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THE HIPPURIC ACID EXCRETION TEST IN PREGNANCY

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IN A PRELIMINARY study¹ the determination of hippuric acid excretion after giving sodium benzoate by mouth, devised by Quick² as a test of liver function, was tried on a small series of normal and toxemic pregnant patients. A high percentage of subnormal values was obtained, and it was indicated that further investigation would be necessary to find, first, if the same results would hold in a larger series, and, second, were this so, if it might be possible to classify the cases with low hippuric acid outputs as to whether the cause lay in impaired production and/or conjugation of glycine with benzoic acid, or in impaired excretion of the formed hippuric acid because of renal dysfunction. Such was the purpose of the present study.

Since his original clinical paper Quick has published a series of additional cases studied by his method,³ and several others have applied the test to some normal patients and to a number with potential or proved liver disease.⁴⁻⁹ There were 5 toxemic pregnant patients in Kohlstaedt and Helmer's series on whom they obtained rather indeterminate results. There is general agreement that the test is practical and is a good index of parenchymal liver function, particularly when used repeatedly to follow the course of disease. It shows adequate correlation with other tests of liver function. It provides no specific index for distinguishing one type of pathology from another. Adlersberg and Minibeck object that the test does not differentiate between disturbed synthesis and disturbed absorption and/or excretion. It is my experience that significantly delayed absorption, as indicated by marked irregularities in the hourly excretion, is exceptional, but it may often be

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an important question whether the conjugated benzoate finds its way through the kidneys at a normal rate. This is particularly pertinent when a condition that affects kidney function such as nephritis, hypertension, or pyelitis exists. Kohlstaedt and Helmer, and Fouts, Helmer, and Zerfas feel that by determining the urea clearance rate in combination with the hippuric acid test the problem of the kidney factor can be largely eliminated. While it is not unlikely that a correlation exists between the index of urea clearance and the rate of hippuric acid excretion, it remains subject to proof. In pregnancy, at least, where so wide a range of maximum and standard urea clearances is found in normal individuals,¹⁰ the approach previously suggested¹ of determining the excretion of hippuric acid given intravenously appeared preferable.

In addition, since the detoxification and excretion of benzoic acid has been shown to depress the excretion of uric acid and to raise the blood uric acid level in nonpregnant individuals,¹¹ it seemed worth while to observe these phenomena in pregnancy.

MATERIAL

The subjects for this investigation were from two sources: a mixed group of multiparas and primigravidas from the dispensary service of Maternity Hospital, Cleveland, some of whom were delivered in the hospital, the rest at home, and a second group of young primigravidas housed from the latter part of pregnancy until after the puerperium at the Florence Crittenton Home, Boston. Random selection was made on the basis of normal physical examination and past history, negative Wassermann tests, and normal pregnancy to the time of testing. It was purposed to study normal pregnancy, but there were some patients who had minor evidences of toxemia overlooked at the time of testing or who later developed toxemia, and these are included as a separate group. No patient was considered normal if she had antepartum albuminuria or a blood pressure of 130/90 or greater, except that transient hypertension at the first visit or during labor was considered normal.

METHOD

Hippuric acid was determined by the modified gravimetric method of Quick.² Urine uric acid was determined by the method of Folin and Wu,¹² blood uric acid by the method of Benedict and Behre,¹³ nonprotein nitrogen by the method of Folin and Wu,¹⁴ and urea nitrogen by the method of Van Slyke and Cullen.¹⁵

The procedure previously described was followed.¹

When urine uric acid was to be determined, the patient was instructed to void and note the time about one hour before she would arrive at the clinic. The bladder was then emptied before giving sodium benzoate and the time interval since the earlier urination calculated. After analysis of this specimen the uric acid excreted in the hour preceding the test could be roughly approximated. After the benzoate was given, aliquot samples for uric acid determination were taken from each hourly urine collection. The amount of hippuric acid thereby subtracted was later calculated and added to each hourly total.

When the excretion of hippuric acid after intravenous sodium hippurate was to be determined, it was found advisable to have the patients drink two glasses of water shortly before the injection in order to have ample specimens.

RESULTS

1. *Excretion of Hippuric Acid After 5.9 gm. of Sodium Benzoate by Mouth.*—Seventy-four tests were completed on 64 normal patients at various periods from the fourth to tenth lunar months of gestation. Twenty-three of these patients had repeated tests in or after the puerperium. In the tabulation 10 antepartum and 3 post-partum observations from the previous study are included. The results, together with other data, are shown in Table I. In order to compress the tables, the

TABLE I. NORMAL SERIES

CASE	AGE	GRAVIDA	GESTA- TION	HIPPURIC ACID OUTPUT AFTER SODIUM BENZOATE†			PER CENT EXCRETION OF I.V. HIPPURATE
				MAX. IN 1 HR.	TOTAL 4 HR.	PER CENT NORMAL	
1. G. L.	19	i	-132* - 18	1.02 1.04	3.08 3.45	102 115	
2. C. McM.	18	i	- 83	0.84	2.84	95	
3. M. G.	24	ii	- 41	0.54	1.32	44	
4. S. S.	19	i	- 65	0.73	2.15	72	
5. H. W.	28	iii	- 53	0.61	0.94	31	
6. M. H.	28	ii	-111 - 29	0.63 0.86	2.18 2.77	73 92	
7. M. D.	19	i	-181 - 41	0.83 0.86	2.58 2.47	86 82	
8. E. I.	24	i	-143	0.51	1.59	53	
9. J. Z.	16	i	- 8	0.61	1.93	64	
10. M. M.	20	i	-182 - 56	0.57 0.68	2.09 1.63	70 54	74.5
11. K. M.	25	iii	-136 - 10	0.86 1.03	2.24 3.40	75 113	
12. M. S.	26	ii	- 58	0.82	1.90	63	
13. E. K.	32	ii	-133	0.67	1.81	60	
14. H. S.	35	ii	-113	0.81	2.71	90	
15. F. T.	20	ii	-111 - 11 - 4	0.54 0.50	2.08 1.77	69 59	73.0
16. H. McM.	23	v	- 73	0.97	3.43	114	
17. D. W.	26	i	-141 - 36	1.01 1.07	3.69 3.78	123 126	
18. J. DeP.	22	i	-106 - 29	1.08 1.01	3.60 3.86	120 129	
19. S. Z.	22	i	-102 - 39	0.38 0.69	0.96 1.71	32 57	
20. L. W.	20	i	- 81	0.98	3.26	109	
21. M. M.	19	i	-121 - 37	0.96 0.93	3.29 2.91	106 97	
22. M. A.	21	iii	- 76	0.61	1.95	65	
23. J. K.	22	i	-123 - 46	0.75	2.52	84	77.5
24. P. G.	24	ii	- 99 - 67	0.77	2.83	94	82.5
25. H. S.	22	i	-131 - 66	0.84	2.95	98	86.5
26. S. Di. T.	23	ii	-150	0.98	3.38	113	
27. A. F.	23	i	-173 -155 -103	0.76 0.88	2.63 2.77	88 92	85.5
28. S. P.	23	i	-142	1.01	3.40	113	
29. A. Z.	22	i	-153	0.80	2.81	94	
30. W. A.	26	ii	-188	0.90	3.40	113	
31. F. E.	22	i	-150	0.72	2.67	89	

*—, Days before delivery; +, days after delivery.

†In grams of benzoic acid equivalent.

‡O. S., from earlier series.¹

TABLE I—CONT'D

CASE	AGE	GRAVIDA	GESTA- TION	HIPPIRIC ACID OUTPUT AFTER SODIUM BENZOATE†			PER CENT EXCRETION OF I.V. HIPPIRATE
				MAX. IN 1 HR.	TOTAL 4 HR.	PER CENT NORMAL	
32. O. S.‡ 2	28	ii	-160	1.14	3.09	103	
33. O. S. 3	22	i	-162	0.99	2.64	88	
34. O. S. 5	21	i	- 1	0.88	2.32	77	
35. O. S. 6	32	i	- 76	0.75	2.26	75	
36. O. S. 10	27	i	- 89	0.96	3.37	112	
37. O. S. 11	26	i	- 36	0.90	2.95	98	
38. O. S. 16	20	i	-200	0.95	2.89	96	
39. M. B.	24	iv	- 78	0.81	3.02	101	
40. R. K.	19	i	- 88 - 86	0.97	3.07	102	81.5
41. E. R.	17	i	- 87 - 80	0.98	2.33	78	72.5
42. M. R.	30	i	- 73 - 71	0.74	2.65	88	76.0
43. H. G.	28	i	-106 -104	0.86	2.79	93	91.5
44. P. M.	15	i	- 60 - 58	0.90	3.26	109	81.5
45. O. S. 7	28	i	- 1 + 10	0.98 1.37	2.35 3.15	78 105	
46. O. S. 9	22	i	- 1 + 10	0.74 1.05	2.36 3.18	78 106	
47. O. S. 12	32	ii	- 8 + 11	1.00 1.03	2.45 2.93	82 98	
48. B. S.	30	i	-103 + 8	0.72 1.16	2.34 3.21	78 107	
49. E. P.	22	i	-155 + 9	0.83 1.32	2.03 3.61	68 120	
50. E. C.	20	i	-148 - 64 - 8 + 9	0.62 0.63 1.04	2.19 2.08 2.38	73 69 79	68.0
51. E. P.	17	i	-103 + 9	0.89 2.62	3.20 3.52	107 117	
52. R. O.	21	ii	- 35 + 8	0.55 0.82	1.59 1.94	53 65	
53. A. B.	20	i	- 83 + 11	0.80 1.09	2.01 2.99	67 100	
54. B. C.	23	i	-117 - 5 + 9	0.50 0.63 0.65	1.50 1.62 2.11	50 54 70	
55. L. R.	18	i	- 95 + 9	0.63 1.11	2.11 3.39	70 113	
56. E. B.	25	i	- 72 - 23 + 10	0.82 0.84 1.20	2.99 2.86 3.53	100 95 118	
57. A. G.	24	i	-102 + 9	0.70 1.10	2.07 2.87	69 96	
58. H. G.	25	i	- 85 + 9	0.73 1.02	2.46 2.61	82 87	

TABLE I—CONT'D

CASE	AGE	GRAVIDA	GESTA- TION	HIPPURIC ACID OUTPUT AFTER SODIUM BENZOATE†			PER CENT EXCRETION OF LV. HIPPURATE
				MAX. IN 1 HR.	TOTAL 4 HR.	PER CENT NORMAL	
59. E. D.	18	i	- 43	0.96	2.87	96	
			- 41				85.0
			+ 30	1.19	3.38	113	
			+ 32				76.5
60. R. L.	16	i	- 38	0.86	2.88	96	
			- 36				77.0
			+ 45	1.11	3.41	114	
			+ 47				73.5
61. M. G.	25	i	- 36	0.60	2.09	70	
			- 34				72.5
			+ 48	1.11	4.11	137	
			+ 50				72.5
62. L. B.	20	i	- 22	1.09	3.20	107	
			- 20				74.5
			+ 55	1.26	4.02	134	
			+ 50				74.5
63. E. S.	16	i	- 63	0.90	2.90	97	
			- 61				90.5
			+ 41	0.96	2.89	96	
			+ 30				73.5
64. E. H.	23	i	- 39	0.84	2.63	88	
			- 37				58.0
			+ 31	1.19	4.06	135	
			+ 33				81.0
65. M. H.	26	i	- 65	0.99	2.92	97	
			- 63				89.0
			+ 19	1.12	4.03	134	
			+ 21				77.5
66. R. T.	16	i	- 58	0.77	2.41	80	
			- 55				72.5
			+ 18	1.00	3.65	122	
			+ 27				84.5
67. M. C.	26	i	- 50	0.67	1.80	60	
			- 48				49.5
			+ 20	0.95	3.39	113	
			+ 27				64.5
68. H. R.	29	i	- 3	0.53	1.79	60	
			- 1				81.0
			+ 46	0.80	2.99	100	
			+ 48				83.5
69. G. D.	17	i	- 3	0.70	2.42	81	
			- 1				78.5
			+ 32	0.98	3.56	119	
			+ 34				78.0
70. R. M.	17	i	- 16	0.82	2.64	88	
			- 14				82.5
			+ 19	1.00	3.56	118	
			+ 21				81.5

excretion for each of the four hours of the test has been omitted, but for each patient the maximum hourly output and the total for the four hours is given. As before, hippuric acid is represented as its gram-equivalent in benzoic acid, and the "percentage of normal" is calculated on the basis of 3 gm., being the average normal nonpregnant four-hour total.

There were 15 ante-partum tests on 13 toxemic patients with 3 repeated post partum. Eight ante-partum and 5 post-partum observations from the earlier series are included with this group. The results are shown in Table II. The toxemia in

most instances was minimal or undeveloped at the time of first testing. The cases have been roughly classified as "Early" or "Late" depending on whether or not evidences of toxemia appeared before the eighth lunar month, and as "mild" unless the blood pressure rose above 160/100 or there were pre-eclamptic symptoms, in either of which latter instances the designation was "severe." The above remarks also pertain to the toxemic group of Table IV.

About half of the patients experienced appreciable reactions of varying degree from the sodium benzoate. A typical reaction consisted of one or more of the following symptoms: flushing, headache, vertigo, tinnitus, and nausea. These effects occurred as often post as ante partum. Tests were interrupted by vomiting eight times. Emesis would probably have been more frequent had it not been possible to persuade other patients not to give in to their nausea. One patient (R. T., No. 61, Table I) who had no reaction at the first test ante partum, when given the benzoate post partum had rather prolonged symptoms and developed a rash and fever lasting two days. It was felt that the severity of the symptoms was contributed to by a mild mastitis, the premonitory signs of which she had failed to report before the test.

In considering the results of the 84 ante-partum sodium benzoate tests on normal patients, it is first to be noted that, while the observations are fairly well scattered through the last two trimesters, there are not enough of them to give valid indications of any progressive trend through pregnancy, which, indeed, could only be well established by repeated interval observations on the same patients from early pregnancy through the puerperium. Of the 14 patients who had repeated ante-partum tests, the division is about equal among those showing significant increase, decrease, or no change.

The average of the 84 observations is 2.57 gm. of hippuric acid as benzoic acid in four hours. This is 85 per cent of normal when compared to the average of 3 gm. in four hours accepted for normal nonpregnant individuals. The lower limit of normal is doubtless under 3 gm., and if we, arbitrarily, take 2.70 gm. as the lower limit of normal we find that but 37 or 42.8 per cent of the tests yielded outputs this great or greater.

The average output of the 26 post-partum determinations on normal patients was 3.22 gm. Of this group but 4, or 15.4 per cent, showed outputs of less than 2.70 gm.

Considering separately the normal patients who had both ante- and post-partum tests (Cases No. 45 to 70, Table I) we find that the ante-partum average of 29 observations on the 26 patients is 2.47 gm. Eight, or 30.8 per cent, excreted 2.70 gm. or more, while, as noted above, post partum, 84.6 per cent excreted 2.70 gm. or more. It should also be pointed out that even though the post-partum test may not in every case have yielded a "normal" value, in only one instance was the post-partum output not greater than the ante-partum output.

When the ante-partum hippuric acid outputs after sodium benzoate are plotted against the weights or surface areas of the patients for whom those figures are available, no correlation is shown, and it can be assumed that the magnitude of variation is greater than could be explained on the basis of individual variation in response due to size.

Before viewing the results of the benzoate tests on the toxemic patients, it should be repeated that this is not a representative toxemic group. Though the cases are too few for definitive analysis, they do show a lower average ante-partum hippuric acid output than the normal group, 2.41 gm., or 80 per cent, of normal, and only 5, or 21.7 per cent, had outputs of 2.70 gm. or better. The post-partum analyses are above the 2.70 gm. level in all but two instances and show increases in all but one.

It is usually considered that the normal individual should excrete at least 0.90 gm. of hippuric acid during at least one of the hours of the benzoate test. When all four-hour total and one-hour maximum excretions reported here are compared, a close correlation is shown between those with normal total outputs and with 0.90 gm. or more one-hour maximums, and between those with low four-hour total outputs and less than 0.90 gm. one-hour maximums. In any one case the hourly output

can be considered particularly significant only if the timing is accurate and the bladder completely emptied at each collection. Under the circumstances of this study it was not possible to control those factors absolutely.

II. *Excretion of Hippuric Acid After 2.0 gm. (2.26 gm. of Sodium Hippurate) Intravenously.*—Hippuric acid excretion as a result of this test was determined ante

TABLE II. TOXEMIC SERIES

CASE	AGE	GRAVIDA	GESTATION	HIPPURIC ACID OUTPUT AFTER SODIUM BENZOATE†			PER CENT EXCRETION OF I.V. HIPPURATE	CLASSIFI- CATION
				MAX. IN 1 HR.	TOTAL 4 HR.	PER CENT NORMAL		
1. A. K.	25	v	-135* - 44	0.48 0.80	1.49 2.54	50 85		LM‡
2. D. R.	22	iii	- 48	1.03	2.53	84		LM
3. A. B.	19	i	- 29	0.84	2.25	75		LS
4. H. S.	26	i	-129	1.14	3.92	131		LM Wass. 4+
5. R. D.	32	iv	- 97 - 93	0.79	2.23	74	51.0	LS
6. P. S.	17	i	- 11	0.63	2.05	68		LM
7. L. B.	35	i	- 73 - 50	0.87	3.06	102	77.5	EM
8. W. F.	24	i	-162	0.73	2.65	88		EM
9. E. S.	19	i	- 6 - 7	0.78	2.56	85	73.0	LM
10. O. S. §17	29	ii	- 7	1.18	3.38	112		EM
11. O. S. 19	31	i	- 1	0.66	1.80	60		LM
12. O. S. 24	42	v	- 39 - 34	1.37	2.76	92	31.0	EM
13. O. S. 1	25	i	- 1 + 11	0.91 1.01	1.86 3.13	62 104		EM
14. O. S. 13	23	i	- 1 + 9 + 8	2.27 1.53	76 3.67	122	79.0	EM
15. O. S. 14	30	i	- 1 + 11	0.75	2.04 2.90	68 97		LM
16. O. S. 18	23	i	- 8 + 10	0.96 1.09	2.46 3.54	82 115		LM
17. O. S. 21	29	i	- 1 + 10	0.82 1.77	2.59 4.07	86 138		LM
18. M. P.	28	i	-101 - 6 + 8	0.89 0.83 0.54	2.52 2.80 0.82	84 93 24		EM
19. C. P.	22	i	-128 + 9	0.54 0.90	1.85 3.08	62 102		LM
20. E. B.	16	i	- 37 - 35 + 53 + 57	0.74 1.10	2.43 3.95	81 132	66.0 89.0	LM
21. M. C.	20	i	- 15 - 13 + 20 + 22	0.60 0.73	1.56 2.65	52 88	50.0 68.5	LS

*—, Days before delivery; +, days after delivery.

†In grams of benzoic acid equivalent.

‡E, early; L, late; M, mild; S, severe.

§O.S., from earlier series.¹

TABLE III. NORMAL SERIES

CASE	AGE	GRAVIDA	GESTATION*	PER CENT EXCRETION HIPPURIC ACID AFTER INTRAVENOUS SODIUM HIPPURATE			
				30 MIN.	30-60 MIN.	60-120 MIN.	TOTAL FIRST HR.
1. M. Z.	35	iii	- 52	54.5	9.0	24.5	63.5
2. I. H.	21	i	-173	70.0	11.0		81.0
3. A. S.	25	ii	- 75	74.0	9.0		83.0
4. E. A.	19	i	- 73	60.0	15.5		75.5
5. E. C.	20	i	- 64	46.5	19.5	9.5	66.0
6. H. H.	23	i	-126	59.5	26.5	19.5	86.0
7. E. C.	28	i	- 90	68.0	14.5	8.5	82.5
8. M. D.	22	i	- 4	52.0	19.0	7.5	71.0
9. R. M.	32	ii	-134	80.0	15.0	6.0	95.0
10. J. K.	18	i	- 18	22.5	39.5	18.5	62.0
11. J. F.	38	iii	- 56	64.0	15.0	5.5	79.0
12. L. M.	37	iv	-126	31.0	38.5	13.5	69.5
13. C. R.	30	ii	-128	62.0	10.0	4.5	72.0
14. R. T.	22	i	-148	78.0	10.0	6.0	88.0
15. M. D'A.	21	i	- 48	54.5	19.0	15.0	63.5
16. M. T.	26	ii	- 34	69.0	16.0	12.5	85.0
17. C. D.	20	i	- 91	47.0	26.0	10.0	73.0
18. E. E.	18	i	- 83	81.0	9.5	3.5	90.5
19. E. A.	21	i	-109	73.0	14.5		87.5
20. F. T.	20	i	- 4	49.0	24.0		73.0
21. I. B.	25	ii	-157	60.0	14.0		74.0
22. J. P.	21	i	- 51	58.0	20.0	13.0	78.0
23. M. M.	20	i	- 56	56.0	18.5		74.5
24. H. H.	29	i	- 59	51.0	31.5	9.5	82.5
25. M. R.	28	v	-108	62.5	18.5	10.5	81.0
26. L. T.	35	vi	- 66	69.0	14.5	6.0	83.5
27. H. S.	32	i	- 68	46.0	40.5		86.5
28. P. G.	24	i	- 67	60.5	22.0		82.5
29. E. P.	37	i	- 55	62.0	21.0	11.5	83.0
30. E. V.	18	i	-165	73.0	18.0	8.0	91.0
31. A. O'B.	26	i	- 73	41.5	31.5	11.0	73.0
32. A. M.	21	i	-152	68.0	13.5	6.5	81.5

*—, Days before delivery; +, days after delivery.

TABLE III—CONT'D

CASE	AGE	GRAVIDA	GESTA- TION	PER CENT EXCRETION HIPURIC ACID AFTER INTRAVENOUS SODIUM HIPPURATE			
				30 MIN.	30-60 MIN.	60-120 MIN.	TOTAL FIRST HR.
33. C. P.	34	vii	- 61	68.5	18.5	9.5	87.0
34. L. S.	21	i	-113	69.0	16.0	6.0	85.0
35. S. F.	24	iv	- 3	56.5	12.0		68.5
36. A. L.	20	i	-123	72.0	18.5	10.5	90.5
37. A. F.	23	i	-103	64.5	21.0		85.5
38. M. S.	27	ii	- 36	76.5	10.5		87.0
39. J. K.	22	i	- 46	47.5	30.0		77.5
40. R. K.	19	i	- 86	55.5	26.0		81.5
41. E. R.	17	i	- 87	36.0	36.5		72.5
42. M. R.	30	i	- 72	46.5	29.5		76.0
43. H. G.	28	i	-106	61.5	30.0		91.5
44. P. M.	15	i	- 62	65.5	16.0		81.5
45. E. F.	17	i	- 53 + 9	59.0 52.0	14.0 16.0	12.5 21.0	73.0 68.0
46. M. B.	26	i	- 46 + 9	50.5 43.0	33.0 20.5	9.0	83.5 63.5
47. E. D.	18	i	- 41 + 32	64.5 61.0	20.5 15.5		85.0 76.5
48. R. L.	16	i	- 36 + 47	40.0 57.0	33.0 16.5		73.0 73.5
49. M. G.	25	i	- 34 + 50	54.5 58.5	18.0 14.0		72.5 72.5
50. L. B.	20	i	- 20 + 50	55.5 59.0	19.0 15.5		74.5 74.5
51. E. S.	16	i	- 63 + 30	71.0 56.0	19.5 17.5		90.5 73.5
52. E. H.	23	i	- 37 + 32	41.5 61.0	16.5 20.0		58.0 81.0
53. M. H.	26	i	- 63 + 21	67.5 56.5	21.5 21.0		89.0 77.5
54. R. T.	16	i	- 55 + 27	21.5 62.0	51.0 22.0		72.5 84.0
55. M. C.	26	i	- 48 + 27	32.0 46.0	17.5 18.5		49.5 64.5
56. H. R.	29	i	- 1 + 48	69.0 66.5	12.0 17.0		81.0 83.5
57. G. D.	17	i	- 1 + 34	61.0 61.0	17.5 17.0		78.5 78.0
58. R. M.	17	i	- 74 + 21	63.5 63.0	19.0 18.5		82.5 81.5

partum on 58 normal patients at various stages of pregnancy, and post partum on 14 of these same patients. Twenty-one ante-partum observations on 19 toxemic patients were obtained, one being repeated post partum, and 4 ante- and 1 post-partum determinations from the earlier series are included. When the patients who were given sodium benzoate also had the intravenous hippurate test, the results of the latter, in the proper time relations, are included in Tables I and II. All of the observations from the intravenous tests are shown in Table III for the normal group and Table IV for the toxemic group.

All of the patients had urine specimens collected at thirty and sixty minutes after injection of the hippurate. On 28 of the normal and 13 of the toxemic patients, the output during the second hour after injection was also determined. The tabulated figures indicate what percentage of 2.0 gm. of hippuric acid was excreted in any one period, and for every case the total percentage in the first hour is given. This last figure is the only one given in Tables I and II.

On scanning the figures in Table III for the percentage excretion of hippuric acid at 30, 60, and 120 minutes after intravenous sodium hippurate given to normal pregnant women, it is apparent that elimination is rapid. The averages are 58.2 per cent for the first period, 20.7 per cent for the remainder of the first hour, and but 10.3 per cent in the 28 instances where the second hour output was analyzed. If it were possible to be sure of a total urine collection for the first half-hour, it is fair to assume that this would be the most significant period. When, however, the urine volume is small, a residual of a few cubic centimeters carries over a high

TABLE IV. TOXEMIC SERIES

CASE	AGE	GRAVIDA	GESTATION*	PER CENT EXCRETION HIPPURIC ACID AFTER INTRAVENOUS SODIUM HIPPURATE				CLASSIFICATION
				30 MIN.	30-60 MIN.	60-120 MIN.	TOTAL FIRST HR.	
1. H. B.	24	i	-117	74.0	5.0	4.5	79.0	L. M.†
2. A. W.	34	ii	- 58	50.0	20.5	13.5	70.5	
			- 30	44.5	17.5		62.0	L. M.
3. L. M.	29	i	- 1	49.0	13.5		62.5	E. S.
4. A. B.	20	ii	- 2	11.0	6.5		17.5	L. M.
5. R. D.	32	iv	- 97	28.5	22.5		51.0	E. S.
6. H. B.	20	i	-152	54.0	22.5	9.5	76.5	L. M.
7. L. B.	35	i	- 50	67.0	10.5	8.5	77.5	L. M.
8. D. H.	28	iv	- 66	66.0	15.5		81.5	E. S.
9. H. Dis.	24	i	- 56	69.0	16.0	8.0	85.0	E. M.
10. E. M.	26	i	- 72	61.0	16.0	11.5	77.0	L. M.
11. P. B.	27	iii	- 64	30.0	39.0	15.5	69.0	E. M.
12. V. S.	23	ii	-120	82.5	17.0	8.0	99.5	E. M.
13. S. E.	19	i	- 7	57.5	15.5		73.0	L. M.
14. L. D.	17	i	- 39	33.5	33.5	14.0	67.0	E. M.
15. E. C.	21	i	-104	67.0	15.5	8.0	82.5	E. M.
16. M. S.	25	i	- 34	48.5	21.5		70.0	E. M.
17. O. S.‡ 18	29	ii	- 2	38.0	15.0	8.0	53.0	L. M.
18. O. S.	20	viii	- 6	30.0	33.0	12.0	63.0	E. M.
19. O. S.	24	v	- 34	11.0	20.0		31.0	L. M.
20. O. S.	23	i	- 1	6.0	23.0		29.0	E. M.
			+ 10	26.0	36.0		62.0	
21. E. B.	16	i	- 35	47.0	19.0		66.0	E. M.
			+ 57	73.0	16.0		89.0	
22. M. C.	20	i	- 13	11.5	38.5		50.0	L. S.
			+ 22	48.5	20.0		68.5	
23. J. R.	27	i	- 14	28.0	28.0	26.0	56.0	L. M.
			+ 10	58.5	25.5	7.5	84.0	

*—, Days before delivery; +, days after delivery.

†E, early; L, late; M, mild; S, severe.

‡O. S., from earlier series.¹

concentration of hippuric acid to the next half-hour. It therefore seems necessary to take the total output of the first hour for the basis of comparison. No relationship was observed between the volume of the urine specimens and their hippuric acid content.

The average first hour excretion for the 14 post-partum observations is 75.1 per cent, and the average ante-partum value for these same patients is 75.9 per cent. Two patients showed increases from low ante- to high post-partum levels, 1 an increase at a high level, 8 no change, and 3 moderate decreases at the higher level.

It would have been of interest, and the data herein presented might have been more significant through comparison, if a series of intravenous sodium hippurate tests could have been made on normal and nephropathic nonpregnant individuals, but such material was not available during the course of this study. While the standard normal excretion rate remains conjectural, the results here given suggest a tentative index of renal function by this test.

On the basis of the present material, a 60 per cent output of hippuric acid in the first hour seems acceptable, subject to further proof, as the lower limit of normal excretion. But 2 of the 58 ante-partum observations on normal patients fall below this level and these rose above it post partum. Two of the post-partum tests yielded values close to but above, the rest well above, 60 per cent.

The toxemic patients (Table IV) show a somewhat lower average first hour ante-partum output, 64.5 per cent, and 6 patients, a considerably higher percentage than in the normal group, fall below the 60 per cent level. Half of the latter had post-partum tests and showed returns to above the 60 per cent level. The small number of cases and the borderline character of the toxemia at the time of most of the tests forbids any assumptions from these figures.

When the first-hour excretion of hippuric acid after intravenous hippurate in the normal patients is plotted against their weights or surface areas a distinct tendency toward an inverse relationship is shown. This would suggest that the rate of excretion of hippuric acid is proportional to its concentration in the body, and that for highly accurate determinations the dose of sodium hippurate should be graduated according to body size. The range of values obtained with the 2 gm. equivalent dose is not great enough, however, to invalidate the present figures.

III. *Excretion of Uric Acid and Blood Chemistry Observations During the Conjugation and Excretion of Benzoic Acid.*—Urine uric acid outputs in milligrams per hour and blood chemistry determinations in mg. per 100 c.c. in Tables I and II, are omitted for lack of space.

The hourly excretion of uric acid before and after giving sodium benzoate was determined ante partum 38 and post partum 6 times on normal patients, and ante partum 8 times and post partum 1 time on the toxemic group.

The urine uric acid shows a rapid fall to a minimum in the second or third hour after sodium benzoate. By the fourth hour excretion has usually begun to rise again. The average uric acid excretion curve for the normal ante-partum group is shown in Chart 1. The few observations post partum and on toxemic patients follow this curve closely. When the normal ante-partum group is divided into those with hippuric acid outputs of more than 2.69 gm. and those with less than 2.70 gm. the uric acid excretion of the former division shows a quicker, of the latter a slower, recovery at the fourth hour.

The effect of sodium benzoate on the twenty-four-hour excretion of uric acid was demonstrated in a forty-eight-hour observation period on one patient (A. F., No. 27, Table I). Chart 2 shows how in the middle of the period during the formation and excretion of hippuric acid the uric acid output is depressed only to become accelerated thereafter, bringing the second twenty-four hours' total to approximately the same level as for the preceding control period.

These results do not differ from those expected in nonpregnant individuals. In any given case the drop in uric acid excretion may be taken as a secondary index of the absorption of the benzoate.

Blood uric acid determinations were made on 26 occasions ante partum and 6 times post partum before and two hours after giving sodium benzoate to normal patients and on 5 and 1 occasions, respectively, in the toxemic group. Analysis of

the normal ante-partum group shows an increase from an average of 2.61 mg. per cent before to 2.82 mg. per cent after the benzoate. In 4 instances there was a decrease, in 1 no change, in the rest increases.

Blood urea nitrogen and/or nonprotein nitrogen was determined simultaneously with the blood uric acids ante partum 20 times. There were some scattered observations post partum and on toxemic patients. These values show a tendency to change

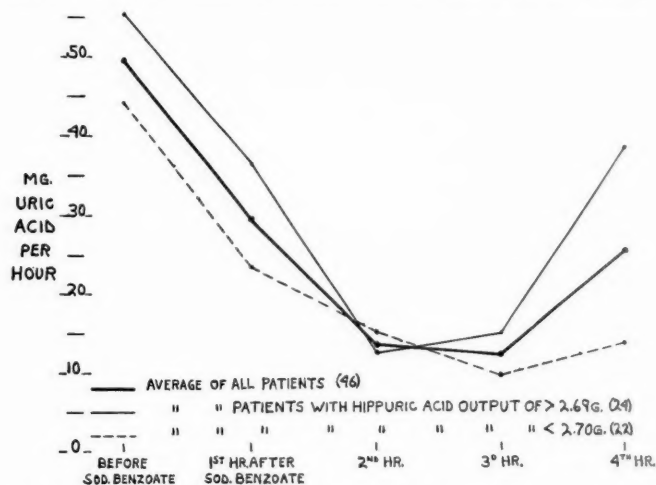


Chart 1.—Excretion of uric acid after sodium benzoate by mouth.

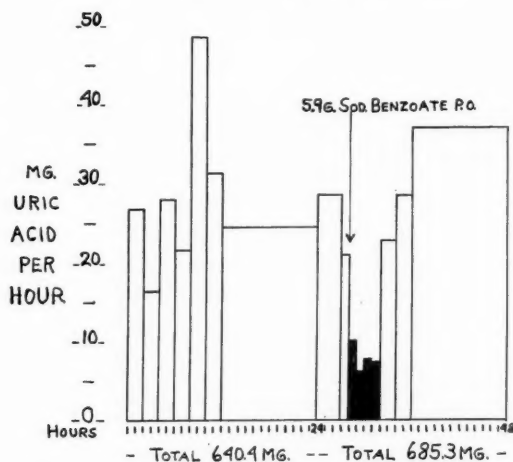


Chart 2.—Forty-eight-hour excretion of uric acid.

in a direction opposite to the uric acid. Seventeen urea nitrogen analyses showed a decrease in the average from 7.27 mg. per cent before to 6.77 mg. per cent at the second hour. Eight decreased, 6 did not change, 3 increased. The average of 16 nonprotein nitrogen values was 23.03 mg. per cent before and 20.95 mg. per cent at the second hour. One showed no change, all the rest decreased.

The significance of the changes in the blood urea and nonprotein nitrogen is not apparent without knowledge of concomitant excretion rates of urea and other nitrogen fractions.

A few blood chemistry analyses four hours after sodium benzoate indicated that the above changes would generally be found more marked at that time.

CONCLUSIONS

It is apparent that a large number of pregnant women exhibit significant deficiency in the excretion of hippuric acid after sodium benzoate is given by mouth.

That this is not usually due to the failure of this substance to pass through the kidneys is predicated by the generally normal excretion of hippuric acid when it is introduced by vein.

The most instructive data of this study are derived from those patients who had both tests ante and postpartum. (Cases No. 59 to 70, Table I; 20 and 21, Table II.) Of the normal group, cases 64 and 67 yielded low antepartum values for both tests, while both tests in both patients returned to normal post partum. One of the toxemic patients (Case 21, Table II) showed low values for both tests ante partum just before the development of severe preeclamptic symptoms. Her intravenous hippurate test was normal post partum, but the excretion after sodium benzoate, while increased, remained subnormal. Although all other patients in these two series had normal ante- and post-partum excretion of the intravenous hippurate, 5 showed subnormal ante-partum excretion after sodium benzoate, returning to normal post partum, and most of those at the normal level ante partum excreted considerably more post partum.

Thus, in the synthesis and excretion of hippuric acid in pregnancy it is possible for either or both phases to be disturbed, and although in the majority of normal cases, at least, there is probably no nephric barrier to hippuric acid, in any one instance a deficient recovery of hippuric acid after sodium benzoate by mouth is not acceptable evidence of a disturbed detoxifying mechanism until it is demonstrated that hippuric acid as such can be freely eliminated. If a low output of pre-formed hippuric acid is found by the intravenous test, that fact may have some significance as an index of renal function, but it becomes impossible to interpret the sodium benzoate test.

The incidence of depressed synthesis and excretion of hippuric acid after sodium benzoate was not related to the well-being of the patients in this group, nor to the development of toxemia or other complications of pregnancy.

It was previously suggested¹ that because of other physiologic changes in pregnancy it might not be strictly correct to interpret this test as an index of liver function. Some other liver function tests seem to give a similar incidence of low values in pregnancy,¹⁶ while still others show no or indeterminate changes.¹⁷ Certainly the application of this test to hepatic disease complicated by pregnancy could be expected to yield considerable confusion, though, even then, repeated tests (with corollary demonstration of adequate elimination of hippuric acid) could have some value in showing progress.

SUMMARY

1. The excretion of hippuric acid after sodium benzoate by mouth was found to be subnormal in more than half of a group of women with un-

complicated pregnancies. A smaller group of patients who developed toxemia showed a somewhat higher incidence of the same depressed function.

2. Post partum the same test shows increased yields of hippuric acid in almost all cases, and, similarly, a return to normal by those giving low ante-partum values.

3. With few exceptions hippuric acid was excreted rapidly when given intravenously as the sodium salt to normal pregnant women. Forty per cent of a small group of toxemic patients showed diminished excretion by this test.

4. The intravenous hippurate test showed no significant changes post partum as compared to the ante-partum results, except in cases having low ante-partum yields when the tendency was to return to normal.

5. The possibility of depressed kidney response to hippuric acid in pregnancy makes it necessary to check renal function in order to interpret the result when a subnormal value for hippuric acid excretion is obtained after sodium benzoate by mouth.

6. Analysis of the urine for hippuric acid after giving sodium hippurate intravenously is recommended as such a check.

7. The ingestion of sodium benzoate in pregnancy is followed by changes in the blood and urine uric acid levels similar to the changes so produced in nonpregnant individuals.

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REFERENCES

- (1) *Hirsheimer, A.*: AM. J. OBST. & GYNEC. 29: 395, 1935. (2) *Quick, A. J.*: AM. J. M. Sc. 185: 630, 1933. (3) *Quick, A. J.*: Arch. Int. Med. 57: 544, 1936. (4) *Vaccaro, P. F.*: Surg. Gynec. Obst. 61: 36, 1935. (5) *Adlersberg, D., and Minibeck, H.*: Ztschr. f. klin. Med. 129: 392, 1936. (6) *Snell, A. M., and Plunkett, J. E.*: Am. J. Digest. Dis. & Nutrition 2: 716, 1936. (7) *Kohlstaedt, K. G., and Helmer, O. M.*: Am. J. Digest. Dis. & Nutrition 3: 459, 1936. (8) *Fouts, P. J., Helmer, O. M., and Zerfas, L. G.*: Am. J. M. Sc. 193: 647, 1937. (9) *Yardumian, K., and Rosenthal, P. J.*: J. Lab. & Clin. Med. 22: 1046, 1937. (10) *Nice, M.*: J. Clin. Investigation 14: 575, 1935. (11) *Swanson, W. W.*: J. Biol. Chem. 62: 565, 1925. (12) *Folin, O., and Wu, H.*: J. Biol. Chem. 38: 459, 1919. (13) *Benedict, S. R., and Behre, J. A.*: J. Biol. Chem. 92: 161, 1931. (14) *Folin, O., and Wu, H.*: J. Biol. Chem. 38: 81, 1919. (15) *Van Slyke, D. D., and Cullen, G. E.*: J. Biol. Chem. 24: 117, 1916. (16) *Sullivan, C. F., Tew, W. P., and Watson, E. M.*: J. Obst. & Gynaec. Brit. Emp. 41: 347, 1934. (17) *Dietel, H.*: Ztschr. f. Geburtsh. u. Gynäk. 113: 209, 1936.

MORBIDITY FOLLOWING RADICAL OPERATIONS FOR PELVIC INFLAMMATORY DISEASE*

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IT HAS always been the policy of the gynecologists at the Mayo Clinic to treat acute pelvic inflammatory disease, when there was no question about the diagnosis, conservatively, employing the medical regimen in vogue at the time. As time went on and as methods of diagnosis and treatment improved, fewer and fewer patients needed surgical treatment. This was especially true of patients with the gonorrheal type of pelvic disease. Since we have had the chocolate blood-agar culture medium to depend on, it has been possible to put many more patients into this definite group. Sulfanilamide, and when that alone fails, added fever treatment, will care for the great majority of early gonorrheal infections before large pelvic masses have developed. If pelvic masses are already present, vaginal Elliott treatment or diathermy will reduce the number of cases requiring surgical treatment. In fact, so much more can be done in a medical way at present for pelvic inflammatory disease that this paper may not seem timely. There are, however, certain types of conditions that will always be surgical problems: those in which the appendix cannot be ruled out, those in which unilateral adnexal disease follows appendicitis or streptococcal infections, and, lastly, those in which patients continue to have symptoms and pelvic masses after a regimen of active medical treatment has been carried out.

One purpose of this investigation was to try to help us decide in this last-named group of cases whether conservative or radical surgical treatment was to be favored. We have been aware that, following conservative surgical procedures, many patients in this group have continued to complain of symptoms similar to those they had prior to operation. Some for a time have had more menstrual irregularity than before operation. We wanted to know whether these symptoms were possibly due to a temporarily disturbed ovarian function due to postoperative inflammation, and what the final outcome was. Of incidental interest was the problem of seeing if we could add anything to our knowledge of the symptoms associated with decreased or failing ovarian function.

We therefore chose a group of cases in which the patients were operated on between Jan. 1, 1925, and Jan. 1, 1935. We felt this would take all of them beyond the so-called latent period following operation which we had noticed lasted in some cases about two years. Every patient in this series, therefore, had been operated upon at least three

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years prior to the time of our follow-up study. The indications for surgical treatment had been inability to control the symptoms or to reduce pelvic masses, or both, by medical means. A few patients had been operated upon early because the appendix could not be ruled out as the primary cause of the condition. The chief presenting symptoms had been the usual ones: pelvic pain (worse with menstruation) and menstrual disturbances, chiefly menorrhagia, and vaginal discharge. A few patients had been concerned chiefly about sterility. In every case there was a fairly good history of pelvic inflammatory disease, the condition having been initiated by a more or less severe attack of pain, with fever, vaginal discharge, and urinary symptoms; the positive pelvic findings were adnexal masses or a tender uterus partially fixed in retroversion with tender palpable adnexa.

Three hundred patients were operated upon during this ten-year period (Table I). We divided this series in several ways, considering etiology, age, and the type of operation (Tables II, III, IV). We have fairly reliable follow-up data on 183 of these patients, which data were obtained on re-examination of the patients, from correspondence, or from a recent questionnaire that was sent out. We are aware of the limitations of this questionnaire method, yet when a patient answers that she has been perfectly well since operation, as many of them in our series did, one would certainly accept the result as satisfactory.

TABLE I. SUMMARY OF MISCELLANEOUS DATA

	PATIENTS
Total operated upon	300
Came to operation with draining fistulas or sinus tracts	15
Died in hospital after operation	7
Developed postoperatively intestinal obstruction	2
Died from obstruction following operation	1
Developed sinus tracts following operation at clinic	3
Developed chronic phlebitis following operation	2
Developed an acute exacerbation following operation	6

TABLE II. TYPE OF SURGICAL TREATMENT WITH REFERENCE TO PATIENT'S AGE AND TYPE OF INFECTION

TYPE OF INFECTION	CONSERVATIVE AGE, YEARS		RADICAL AGE, YEARS	
	-30	+30	-30	+30
Appendiceal	7	4	1	
Postabortal	12	8	2	1
Gonorrheal	4	6	5	5
Indeterminate:				
1. Within 2 weeks after onset*	10	9		3
2. Two weeks to 6 months after onset	7	15	3	7
3. Six months to 1 year after onset	11	11		2
Old infection	24	17	2	7
Total	75	70	13	25

*Of pelvic inflammatory disease.

Though we have presented in Tables III and IV only the final complaints of the patients after at least a three-year period, we have records of the complaints of many of them for the first two years after the operation. These data bear out our surmise that for a certain period following a conservative pelvic operation for pelvic inflammatory disease, the patient often continues to have pelvic symptoms characterized by menstrual irregularities, and particularly, menorrhagia. This latter is the most usual symptom complained of; it occurred in more than 10 per cent of our cases and was no doubt due to the inability of the disturbed ovaries to function normally. Other patients complained of pelvic pain and backache, worse with the menses, and of a discharge. When a woman continues to have any of these troubles following a pelvic operation, she becomes very discouraged. If only the discharge continues, it of itself is annoying enough to make her feel she has not been cured. It may be only a vaginitis due to *Trichomonas* or *Monilia*, and while the surgeon could not cure it, he nevertheless gets the blame for not having done so.

TABLE III. MORBIDITY FOLLOWING CONSERVATIVE OPERATIONS FOR PELVIC INFLAMMATORY DISEASE

OPERATION	PATIENTS	POSTOPERATIVE COMPLAINTS			SUBSEQUENT TREATMENT NECESSARY		PREGNANCIES
		IRREGULAR MENSES	DISCHARGE	PELVIC PAIN	SURGICAL	MEDICAL	
Plastic operation. No organs removed	10	1	1	3		1	
Removal of one tube	9	2	5	6			2
Removal of adnexa on one side	49	11	13	19	7	3	14†
Removal of both tubes	21	9	7	12	1	4	
Removal of tubes and one ovary	43	15	13	21	3	3	
Removal of both tubes and ovaries	13	4	3	4	2	4	
Total	145	42	42	65	13*	15	16

*Minor operations only (dilatation and curettage) in 3 cases; in remainder, surgical procedures.

†Ectopic in 1 case.

TABLE IV. MORBIDITY FOLLOWING RADICAL OPERATIONS FOR PELVIC INFLAMMATORY DISEASE

OPERATION	PATIENTS	POSTOPERATIVE COMPLAINTS			SUBSEQUENT TREATMENT NECESSARY	
		IRREGULAR MENSES	DISCHARGE	PELVIC PAIN	SURGICAL	MEDICAL
Removal of organs except one ovary	20	0	4	4	0	1
Removal of all organs,* panhysterectomy	18	0	4	3	0	2
Total	38	0	8	7	0	3

*Subtotal hysterectomy in 2 cases.

In cases in which one ovary or a part of one ovary and the uterus was preserved, the patients apparently have had the most stormy postoperative course; it usually takes several months to get them righted, if indeed they ever do. They will often present, for a time at least, all of the symptoms associated with failure of ovarian function: menstrual irregularities, oftener of the menorrhagic but occasionally of the amenorrheic type; soreness of the breasts before periods, dysmenorrhea, premenstrual nervousness and depression; headache with the periods, and vasomotor disturbances following the periods. One of the most distressing of these postoperative complications is menorrhagia. In our group of cases 33.3 per cent of the patients complained of irregular bleeding postoperatively. Would it not be well to avoid this complication by removing the uterus too, since it is of no more functional value after bilateral salpingectomy? Our figures show that hot flushes were increased only 10 per cent in those women whose uterus was also removed. After a time the ovary, if there is sufficient good tissue left in it, will begin to function more normally and these disturbances do tend to disappear.

Considerable can be done in a medical way to tide these patients over this so-called latent period. The menorrhagia can often be controlled with luteal hormone and calcium, and the ovarian circulation can be improved by vaginal heat, which likewise helps the pelvic pain, soreness and backache, and at times the residual discharge. If the cervix has not been cauterized at the time of operation, cauterization, carried out in the office, may later be necessary. We believe that when conservative surgical treatment is being contemplated, or after it has been carried out, it is wiser to tell the patient that it may be some time before her periods become regular and that she may need further medical treatment.

Another interesting supposition has been supported by our follow-up study: Women who have pelvic inflammatory disease, and who have had (and sometimes have not had) surgical treatment, are very likely to reach the menopause earlier than other women. Six of our 10 patients who had only plastic operations reached the menopause before forty-two years of age. By a "plastic operation" we mean that neither ovary was entirely removed though in a few cases resection was employed. One patient ceased menstruating at the age of twenty-seven and one menstruated only once after her operation at the age of twenty-eight.

This last woman's case was interesting. She had had her appendix and part of an ovary removed seven years prior to her pelvic operation at the clinic. Three years later she had had a spontaneous miscarriage, after which she had an attack of lower abdominal pain with fever and discharge. She continued to have more or less constant lower abdominal discomfort, worse with the menses, and a profuse menstrual flow lasting from eight to ten days. When the surgeon explored the pelvis he performed only an internal shortening operation. A note was made at the time that there was evidence of chronic pelvic inflammation but the fimbriated ends of the tubes were open, so they were left undisturbed. This was in July, 1926. In October the patient wrote that the operation "had done no good." She was having pain and

had menstruated only once. In May, 1929, she wrote again that she was still having discomfort. In the recent questionnaire we sent her, however, she said she had never had any periods since the operation nor had she had any hot flushes; in other words, ten years after the operation she had no complaints at all.

There were 132 cases in which enough ovarian tissue and uterus were left so that the menses could continue. Twenty-six of the patients, however, had ceased menstruating and were having hot flushes before the age of forty years. One of these patients, who had been operated upon for unilateral adnexal disease, had a normal pregnancy, labor, and parturition at the age of thirty-four years. Her periods were irregular after this. She is now forty-one years old and has had a few hot flushes in the past two years. The number of those whose menses ceased early is higher than the number of those who had flushes; in fact, not one woman in this group who had ceased menstruating complained much of flushes. In contrast to those who ceased menstruating, we would like to mention one patient in this group who was operated upon in 1926 at the age of thirty-two years.

She had been ill for eight months before operation. The surgeon removed both tubes and ovaries, transplanting what he felt was still good of the right ovary into the right rectus muscle. The patient returned to the clinic in March, 1928, two years later, because she had found a small lump in her breast. At this time she said her menses had been regular, lasting two days, but that for the seven months previously she had been having some irregular bleeding between periods. There was a firm nodular uterus (so described by the examining doctor) and in the right rectus muscle was palpable a small mass measuring 2 by 3 cm. No mention was made regarding any tenderness or swelling of the mass with the menses. Nothing was done about the irregular bleeding, it being considered to be due to small fibroids. The small tumor in the right breast, which was benign, was removed. When last heard from (in May, 1938), nearly twelve years after her operation, this patient said that her periods were regular and that she had had no hot flushes and had no other complaints. One would hardly expect the transplanted ovary to carry on so well but this occasionally must happen.

Naturally in this whole group were women with extremely acute pelvic inflammatory disease who were operated upon early when it was not possible to dissect out structures.

One woman, only twenty-two years of age, was operated upon in 1931. She had had trouble for four months. She mentioned in the questionnaire having had a few hot flushes. Another patient, twenty-three years old, who had had trouble for five years (gonorrhea) was operated upon in 1930 for bilateral tubo-ovarian abscesses; these were drained twice before the radical operation was carried out. This patient said in the questionnaire that she had had no flushes or other complaints and was married. It is possible, of course, that she may have a piece of ovary left.

Comparing the group of cases in which one ovary and the uterus was left with the so-called radical group in which everything was removed except one ovary, 21 per cent of the patients who underwent conservative surgical treatment and in whom the uterus was left had hot flushes early and 31 per cent with only an ovary left had an early menopause. None of these patients complained much of the hot flushes.

The small group of 13 patients in whom the tubes and ovaries were removed, but in whom the uterus was left, was very interesting. In all these cases the disease was extensive and large tubo-ovarian abscesses were present. That was the reason for leaving the uterus. Three of these women stated in the recent questionnaire that they were still having regular periods and no hot flushes. Another patient had regular periods for seven years (1927 to 1934) after her operation, and has had no flushes; the surgeon made a note that he thought that he had removed both ovaries but that there was so much infection he could not be sure of this. Four women had irregular bleeding after the operation; 2 of these had to undergo hysterectomy (elsewhere), and 2 had to be given radium (also elsewhere). Of the whole group of women, those who complained most of flushes were the remaining women in this group who had both ovaries removed and those of a second group who underwent panhysterectomy. This would be expected, yet 6 women out of 18 who underwent panhysterectomy apparently had no hot flushes after operation, though 31 per cent of these patients were operated upon before they were thirty years of age. Strange as it may seem, only 1 patient complained bitterly of flushes, saying that they had occurred every forty-five minutes for nine and a half years; this patient was thirty-seven years of age when operated upon.

Our results have substantiated the fact that when both tubes are involved in the inflammatory process it is unusual for pregnancy to occur. In all of our cases in which pregnancy occurred, one adnexa only was involved. In 10 of these cases the etiologic factor was definitely either appendiceal or the infection developed post partum, 2 patients had apparent gonorrheal infection though this was not proved, and in 1 case it was impossible to tell what the cause of the condition was. It is interesting that of all the patients with proved gonorrhea, every one was found by the surgeon to have both tubes involved. Both tubes were removed in every case except one, that of a woman operated upon in 1931 at the age of thirty-one years who had suffered from the disease for nine and a half years. Because the left tube appeared to be in fair condition, it was left undisturbed. This woman recently reported that she had not become pregnant and still had a pain in her left side similar to that which she had had in her right side before her operation.

In our final results of morbidity we considered only those complaints that seemed directly referable to the pelvic organs, such as menstrual irregularities, too frequent or too profuse periods, pelvic pain similar to that before operation or pain made worse by menstruation, continuance of a troublesome discharge, exacerbations of the infection (which occurred in six instances), or whether further active medical treatment or operation had been necessary. We have not considered the vasomotor disturbances or any subjective symptoms.

COMMENT

We would like to make a few comments only in summary as we have not followed a sufficiently large series of patients as yet to feel justified in drawing positive conclusions. Our statistics seem to reveal:

1. So-called plastic operations on the pelvic organs after pelvic inflammatory disease are useless, especially plastic operations on the tubes. Pregnancies do not follow and the patient is often not relieved of her symptoms.

2. There is a definite morbidity after conservative operations for pelvic inflammatory disease but, in the future, with all the means at our command, this should be less than it has been in the past. Good medical treatment before and following such conservative surgical treatment should lessen this morbidity.

3. When there has been extensive pelvic inflammatory disease, with apparent involvement of the ovaries as well as the tubes so that little good ovarian tissue is left, it would seem best to remove the uterus, leaving the patient what ovarian tissue can be left. This saves her from having irregular, often profuse and painful periods. We feel that it is better to save the uterus if there appears to be reason to believe that one ovary will function normally, but it would appear as if several of the women in this series with only one ovary and the uterus left would have been better off with the uterus out. One young woman in our series was so operated upon at twenty-eight years of age (in 1926) after ten months of invalidism following a septic abortion and with all the active treatment we knew at the time to give. She married at the age of thirty-two and says her sexual life is normal. She also says that she has never had any hot flushes.

4. Unilateral pelvic inflammatory disease is usually the result of appendiceal or post-partum infection and, when such is the case, the removal of the affected adnexa improves the patient's general and pelvic conditions and her chances of becoming pregnant.

Mekler, A.: Experiences with the Hormonal Pregnancy Reactions of Aschheim-Zondek and Friedman-Lapham, *Monatsschr. f. Geburtsh. u. Gynäk.* 107: 257, 1938.

In the Zürich University Woman's Clinic 1,360 hormone pregnancy tests were performed from 1930 to 1935. Of this number 676 tests were performed on mice and 684 on rabbits. The mouse test was correct in 96.6 per cent of the cases and the rabbit method in 93.1 per cent. If the doubtful reactions are eliminated the respective percentages are 97.8 for the mouse and 97.4 for the rabbit tests. Both tests are positive in a large proportion of pregnancies within eight days after a missed period. In cases of abortion and ectopic pregnancy the positive reaction disappears proportionately to the severity of the symptoms. If an abortion is rapidly completed or an ectopic pregnancy quickly removed, the tests become negative very quickly. The author believes that both tests should be employed. In most cases of pregnancy the mouse test should be used but where it is important to obtain a rapid result the rabbit test is preferable.

J. P. GREENHILL

THE MANCHESTER (PARAMETRIAL FIXATION) OPERATION FOR CURE OF PROLAPSE AND CYSTOCELE*

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IN 1888, Donald of Manchester, England, began to treat uterine prolapse by combining anterior and posterior colporrhaphy with amputation of the cervix. Previous to this, the operative procedures utilized in curing prolapse consisted either of some sort of vaginal shortening or of cervical amputation, but very seldom a combination of the two. As a matter of fact it is interesting to note that before the turn of the last century, the majority of cases of prolapse were not treated surgically at all. Pessary insertion was the method commonly employed, and perineorrhaphy was done on occasion to enable the patient to wear a ring pessary. At present, the indication for the use of the pessary should be limited to patients, young or old, who suffer from medical diseases contraindicating surgery.

The variety of operative procedures used in curing uterine prolapse is testimony to the fact that for many years no one method applicable to the great majority of cases has been developed. The choice of operation has usually been determined by the age, parity, and social status of the patient. Vaginal, abdominal, or a combination of the two methods of surgical approach have been utilized with varying degrees of success.

The operations devised for the cure of prolapse which are most commonly employed today include vaginal hysterectomy, Watkins interposition operation, abdominal fixation of the uterus, LeFort's colpoeleisis, and colporrhaphy. The objections to the fixation operations are obvious to all gynecologists who have had experience with these methods. In a series of 200 ventrofixations cited by Frank, 21, or 10.5 per cent, developed postoperative ventral hernia. Vaginal hysterectomy carries with it a mortality of 1 to 2 per cent. Aside from this, extirpation of the uterus removes the best anatomic support for the bladder. It is not unusual in our clinic to find recurrent cystoceles in spite of high, well-supported vaginal vaults following vaginal hysterectomy; and post-operative prolapse of the vaginal vault taxes the resourcefulness of the best gynecologist. Further, removal of the uterus in premenopausal years causes a cessation of menstruation, with its attendant psychic disturbances; and hastens the climacteric. Kretzschmar and Gardiner have shown that hysterectomy with ovarian conservation in women thirty-six years of age or less was followed by menopausal symptoms before 40 years of age in approximately 60 per cent of the patients. Vaginal hysterectomy for the treatment of prolapse is best adapted when there is associated uterine pathology. The Watkins interposition operation

*Presented before the Chicago Gynecological Society, May 20, 1938.

has given good results in the treatment of prolapse, but the procedure involves invasion of the peritoneal cavity and may require sterilization. It is also important that the uterus be neither too small nor too large in order to fit properly into the pubic arch, and amputation of the cervix is usually necessary for a good result in a large percentage of the patients. The LeFort colpocleisis operation has obvious limitations, but where indicated, gives gratifying results. Anterior and posterior colporrhaphy alone tighten the weakened pelvic fasciae, but the presence of an elongated cervix acts as the long arm of a lever which brings the long axis of the uterus into a line with the vaginal axis and thus predisposes to recurrent prolapse.

In 1928, Baer and Reis analyzed 220 operations for prolapse performed by members of the gynecologic staff of the Michael Reese Hospital. The operation most often employed in this series was the Watkins interposition operation, performed in 91 patients, with complete success in 87.5 per cent of the cases. There was one death and the gross morbidity was 55.1 per cent. In 1937, Baer, Reis, and Laemmle analyzed a subsequent comparable series of prolapse cases and found that the trend in the treatment of uterine prolapse at the Michael Reese Hospital in ten years had shifted from the interposition operation to vaginal hysterectomy. The results of this operation showed success in only 70.7 per cent. There were 2 deaths and a gross morbidity of 50 per cent. As the authors point out, the operation to which the staff turned to improve its results in the cure of prolapse, namely, vaginal hysterectomy, was attended by a much smaller percentage of cures (70.7 per cent) than the operation used most often previously, namely the Watkins interposition operation (87.5 per cent).

In recent years, the staff at the Michael Reese Hospital has utilized the Manchester operation as the procedure offering the best results in the greatest number of cases. The attention of the medical profession in this country was first directed to this operation by Frank, who in 1932 published a preliminary report. In this article, the author reviewed a large series of cases of prolapse treated by a variety of other operations. The results in this group were satisfactory in 66 per cent of the patients and good in only 46 per cent; and because of this the need for a better operative treatment was stressed. Mestitz in 1932 also described an operation similar in principle to the Manchester and used by Halban in his clinic since 1919. The Manchester operation has been employed for the treatment of prolapse in the British Isles for over forty-five years, having been introduced by Donald, and reported on at various times by Fothergill and Shaw.

Between Dec. 15, 1935, and Jan. 1, 1938, there were 51 Manchester operations performed at the Michael Reese Hospital by seven operators. The operations so classified were those in which the typical parametrial fixation stitch was used. In our analysis of case records we found many patients scheduled for Manchester plasties preoperatively, but since the actual surgical procedure did not include parametrial shortening, we did not include them in our series. The parametrial fixation was most commonly performed in association with cervical amputation but in a few cases the cervix was left in situ.

The chief primary indication for the performance of the Manchester operation is prolapse of the uterus. It is often difficult to agree on the

exact extent of uterine prolapse in any given patient, since variations in the size and length of the cervix influence the opinion of the examiner. It is not uncommon to find divergent opinions as to the degree of prolapse expressed by various examiners, when the patient is examined more than once. Fear, nervous tension, etc., may cause marked contraction of the voluntary muscles in the pelvic and urogenital diaphragms and thus prevent the uterus from descending with strain. On the other hand, if the patient is completely relaxed at a subsequent examination, the cervix may descend far beyond its former position. We have repeatedly witnessed the appearance of the cervix beyond the vestibule under general anesthesia where previously the most severe straining by the patient did not deliver it out of the vagina. On our service, we classify as first-degree prolapse, descent of the normally-sized cervix to the level of the ischial spines; second-degree prolapse, descent to the vestibule; third-degree prolapse, descent outside the vagina; and procidentia or complete prolapse, descent of the corpus uteri outside the vagina. It is obvious that a uterine corpus may be normally placed, but its elongated or hypertrophied cervix may protrude from the vulva. The over-sized cervix is tissue below the insertion of Mackenrodt's ligaments into the uterus and since the parametrium is intact, the uterine prolapse is in reality only apparent. Clinically, however, the symptomatology and treatment is similar to cases of true prolapse. The performance of parametrial fixation with cervical amputation in cases of elongated and hypertrophied cervix is valuable, in that it sharply anteflexes the remaining corpus, thus preventing descensus.

In our series of 51 patients, the primary indication for performing the Manchester operation was uterine prolapse in approximately four-fifths of the cases (41 or 80.4 per cent). Elongation of the cervix was a very frequent accompaniment of the prolapse. Hypertrophied, elongated, and lacerated cervix was the primary operative indication in 4, or 7.8 per cent, of the cases, and cystocele was the primary operative indication in 6, or 11.8 per cent. Cystocele, in itself, is probably the most common form of pelvic prolapse. Its production during labor, implies a break at the so-called "weak-spot" in the uteropubic fascia, and since this fascia is continuous with the fascia incorporated in the bases of the broad ligaments, the bladder hernia may be a forerunner of true uterine prolapse. Prolapse of the bladder, furthermore, increases the

TABLE I. INDICATIONS FOR MANCHESTER (PARAMETRIAL FIXATION) OPERATION

PRIMARY INDICATIONS	NO.	TOTAL %	ASSOCIATED PATHOLOGY				
			CYSTO.	RECTO.	ELONG. CERVIX	HYPERT. CERVIX	LAC. CERVIX
Uterine prolapse	41	80.4					
First-degree	10		10	9	6	1	8
Second-degree	18		18	15	10	1	10
Third-degree	12		12	11	9	1	10
Procidentia	1		1	1		1	
Cervical pathology	4	7.8	1	4			
Elong.; Hypert.; Lac.							
Cystocele	6	11.8		6	1	1	4
Total	51	100					

vesicouterine space interperitoneally, allowing bowel to be interposed between uterus and bladder. This causes the corpus to fall back into a position of retrodisplacement, which constitutes the first stage in uterine descent. In the patients with cystocele as a primary indication, cervical amputation was done in 4 and the cervix allowed to remain in situ in one. There were 4 other patients in whom the cervix was not removed; 2 with first-degree prolapse and cystocele; 1 with second-degree prolapse and cystocele; and 1 with third-degree prolapse and cystocele. All the cases of prolapse were associated with cystocele.

Parturition is not necessarily an essential predisposing factor of prolapse, which occasionally occurs in nulliparas. Heavy industrial occupations may predispose to descensus in these women by increasing the intra-abdominal pressure or weakening the pelvic floor. Also some patients may manifest a congenital weakness of the fasciomuscular system. Three of the patients in our series with prolapse were nulliparas. One was 51 years of age, and single, who upon straining could deliver the cervix beyond the vestibule. This prolapse was associated with marked pelvic floor relaxation, and a huge cystocele and rectocele. X-ray of the lower spine revealed an occult spina bifida. Another was 23 years of age, married, and manifesting a second-degree prolapse. The third, aged 49, had an elongated cervix with cystocele and rectocele, the cervical pathology being on the basis of an old chronic endocervicitis. The remaining patients were parous, the number of full-term births ranging from 1 to 11 with an average of 3. The youngest patient was 22 years of age, and the oldest 69, the average age being 43. Four patients were under 30 years of age; 14 were between 30 and 40; 20 were between 40 and 50; 11 were between 50 and 60; and 2 were over 60 years of age.

TECHNIQUE OF OPERATION AND RESULTS

The following description is our modification of the original Manchester technique. After the usual preparation as for any vaginal operation, the cervix is grasped with a vulsella and pulled down into the introitus. An inverted "T" shaped incision is made, starting just below the external urinary meatus and circumcising the cervical vaginal mucosa just above the external os. The posterior portion of the circular incision is not completed until the pubocervical fascia has been reconstructed in order to conserve blood loss from the posterior flap. The flaps are dissected laterally exposing the bladder with its overlying weakened uteropubic fascial layer. This is accomplished first by sharp and then by blunt dissection. Marked venous bleeding is usually encountered far laterally and this should be controlled by suture before proceeding. The bladder is next freed from the anterior wall of the cervix and pushed upwards by blunt finger dissection. This maneuver makes prominent the "bladder pillars" of uteropubic fascia on either side (Fig. 1). The angles of the bladder must be carefully dissected upwards in order that the ureters may be completely removed from the danger of ligation (Fig. 3). The bladder hernia is then reduced by uniting the uteropubic fascia with interrupted Lembert's sutures of catgut. Interrupted silk sutures are placed in two planes in the region of the internal vesical sphincter if incontinence is a prominent symptom.

The bladder pillars of each side are caught between two clamps at a level of 1 cm. above the plane of cervical amputation. The top one is placed well laterally and takes in its grasp some cervical and parametrial tissue (Fig. 2). When ligated, this stitch includes fibers of parametrium and uteropubic fascia and marks the location for the parametrial stitches to be placed later on.

The vaginal mucosa is then dissected free from the cervix laterally and posteriorly, and a hemostatic suture is placed on each side, ligating the cervical branches of the

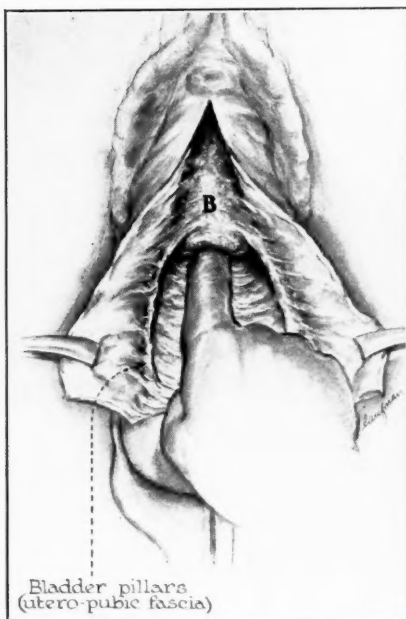


Fig. 1.

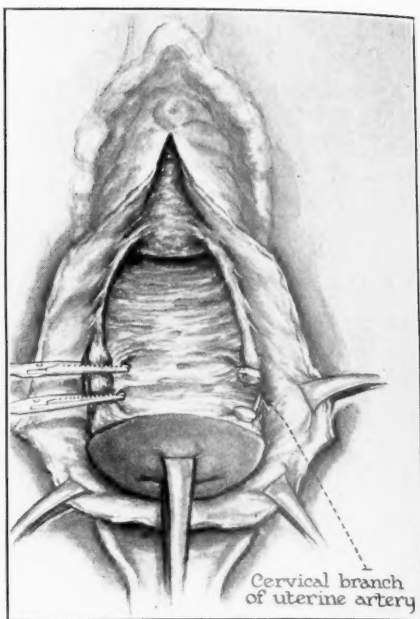


Fig. 2.

Fig. 1.—After an inverted "T"-shaped incision, the bladder is freed from the cervix and dissected upwards, making prominent the lateral portions of uteropubic fascia ("bladder pillars").

Fig. 2.—The "bladder pillars" are clamped, cut, and ligated, the upper clamp including parametrium laterally and some cervical tissue.

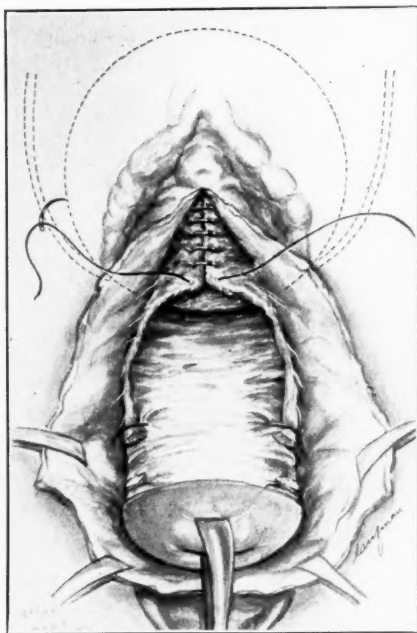


Fig. 3.

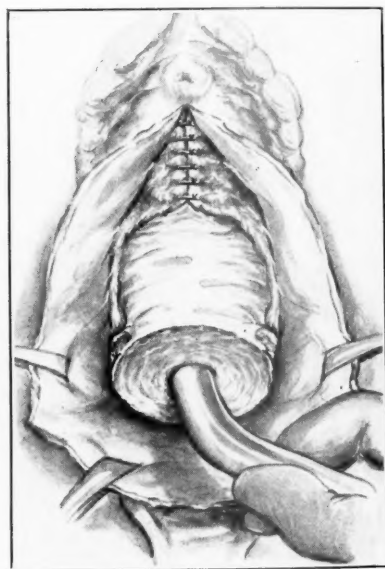


Fig. 4.

Fig. 3.—Illustrating the high position of the ureters away from possible ligature, when the bladder "corners" are carefully dissected upwards.

Fig. 4.—The cervix has been amputated and dilatation and curettage is performed through the clean stump.

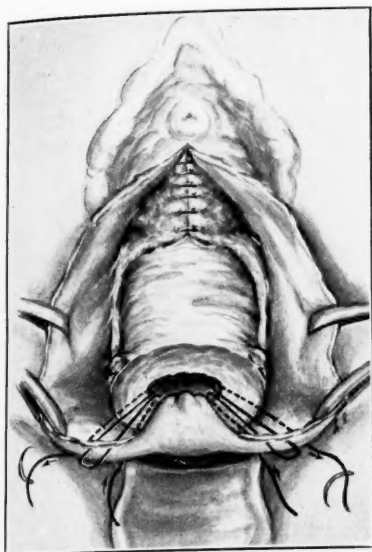


Fig. 5.

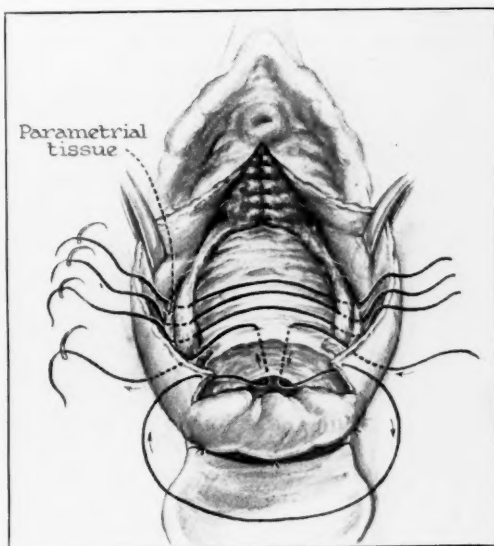


Fig. 6.

Fig. 5.—The posterior and the medioposterior inversion stitches are placed as indicated. This facilitates the placing of the parametrial stitches.

Fig. 6.—The anterior inversion stitch is placed, but not tied until the parametrial stitches are inserted. The parametrial stitches are placed to include the tissue just lateral to the fixed fibers of the uteropubic fascia.

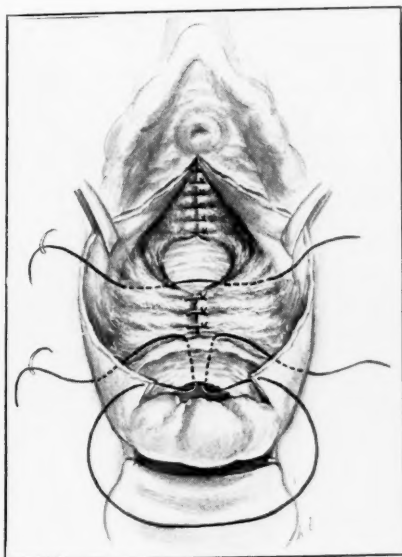


Fig. 7.

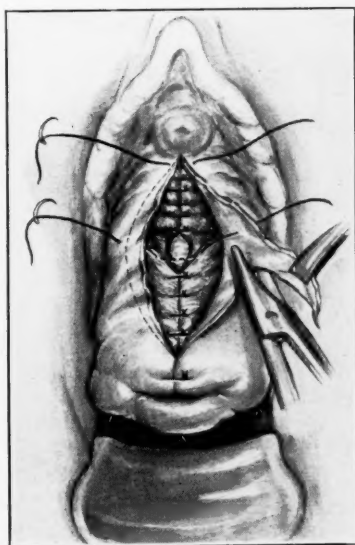


Fig. 8.

Fig. 7.—The parametrial stitches are tied in front of the cervix forcing it backwards. The remaining uteropubic fascia is united in the midline and includes uterine tissue.

Fig. 8.—The vaginal mucosa is trimmed elliptically as indicated. A few interrupted sutures angulate the vaginal mucosa on the uterus, thus further supporting the bladder.

uterine arteries at a level just above the plane of amputation. If a low cul-de-sac is opened into, the peritoneal cavity is closed by a purse-string suture high on the posterior surface of the uterus. The cervix is then amputated circularly or by conical excision. After this, the remaining cervical canal is dilated to a number 12 or 16 Hegar and the endometrial cavity briskly curetted (Fig. 4). Dilatation and curettage after cervical amputation rather than before is not only a simpler and a safer procedure but removal of the infected lower cervix also obviates the forcing of the infectious secretions into the uterine cavity. Wide dilatation also facilitates a more proper inversion of the vaginal mucosa into the cervical canal.

The vaginal mucosa is then inverted into the canal by modified Sturmdorf stitches placed posteriorly and posteriomediaally as indicated (Fig. 5).

The parametrial fixation stitches are next placed and include on each side, the parametrial tissue just lateral to the transfixed uteropubic ligaments. These are not tied until the anterior inversion stitch for the vaginal mucosa is placed (Fig. 6). Tying the fixation stitches unites the parametria in front of the remaining cervix, forcing it backward and anteflexing the corpus (Fig. 7). The cervical reconstruction is then completed by tying the anterior vaginal inversion stitch.

The remaining uteropubic fascia is then united in the midline, including the uterine tissue below the bladder level in order to lend further support to that structure. The vaginal mucosa is then trimmed and united in the midline (Fig. 8).

A perineorrhaphy is usually performed including reconstruction of the levator "sling," to add further support to the pelvic viscera.

The morbidity following this operation is unusually slight, and the great majority of temperature elevations was accounted for by urinary tract infections. Out of 51 patients, excluding urinary retention as a morbidity, 15 (or 29 per cent) developed morbid conditions as listed in Table II. There was no mortality. Fourteen

TABLE II. MORBIDITY IN 51 MANCHESTER OPERATIONS

	NO.	PER CENT
Cystitis	12	23.0
Pyelitis	8	15.0
Parametritis	2	3.0
Thrombophlebitis	1	1.9
Wound infection (perineum)	4	7.0
Secondary hemorrhage	1	1.9
Total Morbid Patients	15	29.0

patients had the Pezzar retention catheter inserted into the bladder following the operation for an average of five days. In this group there were 10 instances of cystitis and 8 of pyelitis. Twenty-eight of the remaining patients had to be catheterized more than once following the operation. There was one case of secondary hemorrhage from the cervix which occurred on the eighth postoperative day. This required ligation of a "spurter" and necessitated blood transfusion. The morbidity from the Manchester operation compares favorably with the morbidity following the two other operations most commonly used for prolapse and cystocele in our institution the past ten years. Vaginal hysterectomy was associated with a morbidity of 50 per cent and some of the conditions such as sepsis and peritonitis were major morbidities. The mortality from this operation was 1.7 per cent. The interposition operation had a gross morbidity of 40 per cent with no mortality (Table III).

TABLE III. COMPARISON OF OPERATIONS FOR PROLAPUS UTERI

OPERATION	CASES	MORTALITY	MORBIDITY	CURES
*Vaginal hysterectomy	116	1.7%	50%	70.7%
*Interposition operation	30	0	40%	89.2%
Manchester operation	51	0	29%	97.9%

*Over ten-year period ending January, 1937 (Baer and Reis).

The pathologic findings in the amputated cervixes revealed such conditions as old erosion, chronic endocervicitis, and Nabothian cysts. Two patients revealed squamous cell hyperplasia of the cervix and one a fibroma. The endometrial curettings were negative except for one case of old retained placenta (asymptomatic). Carcinoma was absent in all specimens.

The average stay in the hospital was twelve days. Eleven patients stayed over two weeks. Of these only 2 remained over eighteen days, one with parametritis, and one with a complete breakdown of the perineal wound.

The results of the operation were uniformly gratifying. All but 2 patients were followed. The period of follow-up postoperatively was as follows: 8 patients examined after twenty-four months; 13 patients examined between eighteen and twenty-four months; 8 patients between twelve and eighteen months; 15 patients between six and twelve months; and 5 patients between four and six months. A patient was declared to have a good anatomic result if the cervical stump was fixed high in the vault of the vagina; if the corpus uteri was anteфлекed; and if there was no prolapse of the anterior vaginal wall. With these as criteria, the prolapse was cured in the entire series with but one exception (97.9 per cent cures). This was in a 54-year-old para v, who entered the hospital with a second-degree prolapse, large cystocele and rectocele and lacerated perineum. Her convalescence was uneventful. Fourteen months postoperatively, the cervical stump descended to the level of the ischial spines and was associated with recurrent cystocele. Salmon reported a series of 254 operations with one case of recurrent prolapse. Four of the 49 followed cases had recurrent cystocele. Since 46 of the followed cases had bladder operations, this represents an anatomic failure of anterior colporrhaphy in 8.7 per cent of the cases. Stricture of the remaining cervical canal was encountered in 2 patients, and this was easily overcome by probing with a uterine sound.

The symptomatic cure was extremely satisfactory. All the patients were relieved of the "bearing down" sensation which was the most common preoperative complaint. The failure to completely cure the symptom of impairment ("stress" incontinence) was manifested in about one-third of the patients who originally complained of this symptom. However, the degree of control was markedly improved in the large majority of these patients.

Pregnancy following the Manchester operation has been reported rather frequently. In 1921, Fothergill, publishing the results obtained in 156 cases, reported two patients who had borne full-term children since the operation. His percentage of cures of prolapse in this series was 97 per cent. Shaw, reporting a large series of cases from the same clinic, cites 18 patients who had borne children subsequent to the operation. Of these 18, 5 or 27.8 per cent, developed a recurrence of the prolapse. These failures were not charged against the operation as they were considered due to a recurrence of the damage which produced the original prolapse. Salmon reports 2 patients who had uncomplicated labors, following the operation. There was no recurrence of prolapse or cystocele in either patient.

One patient in our series became pregnant one year after the operation. She was a para iv who had had quick labors previously, but the duration of the first stage in this labor was eighteen hours. The delivery was spontaneous, but complicated by a second-degree laceration of the perineum. Postnatal examination six weeks after delivery revealed a recurrent cystocele, but the uterus remained high.

Sterilization was performed in 4 of the 51 patients. In 3, the Madlener technique was used and in one cornual excision was done. Since the average age of our patients was 43, the necessity for sterilization was not frequently considered. In young women with large families, sterilization is a wise and often welcome additional procedure.

CONCLUSIONS

1. The Manchester operation is the best method of treatment for prolapse and cystocele in the large majority of patients, young or old.
2. The technique is readily acquired and is both anatomically and physiologically sound.

3. A cure of 97.9 per cent in prolapse by use of this operation definitely establishes its superiority over other methods of operative treatment.

4. The morbidity is low and is usually confined to urinary tract infection. There is no mortality.

5. The operation does not preclude future pregnancy and labor.

6. A modification of the original Manchester technique is described.

REFERENCES

- (1) *Donald, A.*: J. Obst. & Gynaec. Brit. Emp. 28: 256, 1921. (2) *Fothergill, W. E.*: Ibid. 28: 251, 1921. (3) *Lacey, F. H.*: Ibid. 28: 260, 1921. (4) *Shaw, W. F.*: Proc. Roy. Soc. Med. 23: 1159, 1930 (Part 2). (5) *Idem*: AM. J. OBST. & GYNEC. 26: 667, 1933. (6) *Frank, Robert T.*: Ibid. 24: 574, 1932. (7) *Idem*: Ibid. 29: 240, 1935. (8) *Kretschmar, N. R., and Gardiner, S.*: Ibid. 29: 168, 1935. (9) *Baer, J. L., and Reis, R. A.*: Ibid. 16: 646, 1928. (10) *Baer, Reis, and Laemmle*: Ibid. 34: 827, 1937. (11) *Mengert, Wm. F.*: Ibid. 31: 775, 1936. (12) *Salmon, U. J.*: Ibid. 34: 58, 1937. (13) *Mestitz, W.*: Surg. Gynec. Obst. 54: 663, 1932.

58 EAST WASHINGTON STREET

DISCUSSION

DR. W. C. DANFORTH.—The procedure which has been described by the essayists for the cure of descensus of the uterus and bladder depends upon the reconstruction of the damaged upper pelvic floor, a name which was given many years ago by Polk to the structures at the level of the upper part of the cervix or lower part of the corpus which support the weight of the uterus. The ligaments of Mackenrodt, the uterosacral ligaments and the pubocervical ligaments or fascia are the more important parts of this structure. Between these ligaments is a network of fascial or connective tissue fibers, the whole making up an upper pelvic floor of which the ligaments just named are merely thickened portions. Injury at this level permits the uterus to descend or allows the bladder to herniate. When injury of the posterior part of the structure has taken place an enterocele follows. Repair of cystocele requires the reconstruction of the anterior part of this supporting mechanism. A true enterocele is not benefited by a repair of the perineum and is only cured by the repair of the posterior part of the upper pelvic floor.

Moderate degrees of descensus have been treated in some American clinics for years by detaching the bases of the broad ligaments and uniting them in front of the upper part of the cervix, with or without amputation of the cervix. This is an effective procedure. The proper restoration of the essential supports of the uterus and neighboring structures should result in relief of the descensus. Reported results from the clinic in which the operation originated as well as others from clinics elsewhere indicate that clinical experience bears this out. We must, therefore, include the parametrial fixation among the operations which may be used for the correction of descensus.

Abdominal operations are very rarely used at present in the treatment of descensus in gynecologic clinics and remain only as a means of treatment in the hands of occasional operators and of some general surgeons. Among the vaginal operations preferences will vary. The results reported in this paper are excellent both as to mortality and morbidity.

In our service we have continued to favor vaginal hysterectomy in our management of marked descensus. I am reporting 90 such cases in a series of 266 vaginal hysterectomies not yet published. In this group three recurrences have been seen, a rather larger incidence of failure than that reported by Drs. Leventhal and Boshes. In our experience, if a marked descensus is present, a considerable part or all of the uterus protruding from the introitus, we frequently find a marked enterocele. Often an important part of the operation is the excision of the pouch of Douglas and the approximation of the uterosacral ligaments in order to close the posterior portion of the upper pelvic floor. In studying the illustrations shown us by Drs. Leventhal

and Boshes I do not find that any part of their operation is devoted to the reconstruction of the posterior structures and this is true of other published reports. I do not find, in the tabulations, any note of enterocele; yet, in any considerable number of cases of marked descensus, the occurrence of this lesion would be expected. I would like to ask whether enterocele was a frequent finding and what the opinion is, in the Michael Reese Clinic, as to the necessity of surgical attention for its correction. In an illustration of an early stage of the operation a significant bulge is seen in the posterior vault which would indicate that the very skillful artist who made the drawings had noticed, or had had her attention drawn to, a more than normal fullness in that area. May I ask whether the support attained by the procedure described is sufficient in all cases to care for any posterior weakness? The colpoperineorrhaphy which accompanies the parametrial fixation will, of course, help in controlling this by the aid it gives in keeping the uterus in anteversion.

The procedure described for the management of the vesical herniation is excellent and the description of the anatomical supports of the bladder is well given. Familiarity with these supports and a knowledge of the mechanism of bladder herniation are essential for effective correction of descensus of the organ. The emphasis which is placed upon the freeing of the bladder at each side before displacing it upwards is wise. This is important in all operations in which the bladder is raised to a higher level. Failure to mobilize the bladder laterally will not only endanger the ureters, as the essayists point out, but may cause the bladder, after operation, to assume a "saddle bag" shape.

The risk of this operation should, as the essayists say, be less than that of the other available means of surgically treating descensus. This fact, together with the very good results which the operation has given in the hands of the staff of the clinic from which this report comes, must cause us all at least to consider parametrial fixation as one of the procedures available for the management of descensus.

DR. N. S. HEANEY.—I like this operation as described tonight very much for cases of marked cystocele and rectocele. I see no need, however, to call this a Manchester operation as all of the Manchester part has been replaced by better procedures, particularly by the step of the bladder advancement. The type of operation to choose in a prolapse depends upon the sort of case which is confronting one. This operation is a good one if the uterus does not protrude beyond the introitus and where a marked cystocele is present. This operation has no place, however, in the treatment of complete procidentia. If a case of procidentia is to be cured by a vaginal operation, the uterus has to be removed so as to get a high anchorage on the ligaments of the uterus for the vagina. The interposition has no place in the treatment of any sort of prolapse or cystocele.

DR. JOSEPH L. BAER.—Twenty per cent of all women normally have a retrodisplacement. The work of Sturmdorff in his studies of pelvic inclination convinces me that this plays a role in the appearance of so-called normal retrodisplacements. Now if that group of young women who first come under our observation with so-called normal retrodisplacement could be followed through into their maturity and middle life, I believe that a goodly proportion of prolapse would be found to arise out of that group of normal retrodisplacements. Occasionally but very rarely we find prolapse with anteflexed or anteverted uterus, but so seldom do we find it that I must protest against ignoring the effect of intra-abdominal pressure in the production of retrodisplacement and its sequela, descensus uteri.

DR. LEVENTHAL (closing).—Occasionally either advertently or inadvertently we open into the cul-de-sac of Douglas and when this is done the cul-de-sac is closed by a purse-string high on the uterine wall.

The interposition operation, we believe, has a definite place in the treatment of prolapse. It is especially valuable in cases of huge cystocele, the corpus uteri acting as a support for the bladder. We have noticed time and again in patients with cystoceles and incontinence that by putting two fingers in the vagina they are able to control the act of urination. The corpus of the uterus acts as a permanent support in these cases, and thus interposition with cervical amputation is a valuable procedure.

THE INFLUENCE OF THE HORMONAL ACTIVITY OF THE
OVARIES UPON THE CHARACTER OF TUBAL CON-
TRACTIONS AS DETERMINED BY UTERINE
INSUFFLATION*

A CLINICAL STUDY

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THE possibility of estimating ovarian function clinically by the character of the rhythmic tubal contractions was suggested in 1927.¹ This assumption was based upon experimental facts and upon observations made with the test for tubal patency. Experimental and histologic studies of Kehrer,² Blair,³ Corner,⁴ R. T. Frank,⁵ S. R. M. Reynolds,⁶ Seckinger and Snyder,⁷ Wislocki and Guttmacher,⁸ Westman,⁹ Manzi,¹⁰ Moir,¹¹ Andersen,¹² Moreau¹³ and Lee¹⁴ and many others have indicated a close correlation between cyclic functional and anatomic changes in the tubes and synchronous processes in the ovary. The material used in these studies consisted in most instances of isolated portions of the Fallopian tube or the whole tube of various species including the monkey. The excised organs were kept in a state of temporary survival.

Rhythmic contractions of extirpated oviducts of the sow have been demonstrated by insufflating oxygen through the attached uterus, while the organs were immersed in Locke's solution at body temperature (I. C. Rubin,¹ Whitelaw¹⁶). The pressure variations were thus recorded as well as the rhythmicity of the contraction waves. Mikulicz-Radecki¹⁵ repeated my experiments and found similar results. In order to see whether there is a similarity between the rate of contractions of the intact oviducts and that of segmented portions, Whitelaw¹⁶ undertook the task of insufflating the uterus and Fallopian tubes of the sow after the manner employed clinically. As the ovaries were available, the particular estral phase could be determined. He found that in most specimens the uterotubal junction during estrus resisted the passage of oxygen to a pressure of 200 mm. Hg. This resistance was due to the presence of hypertrophied lymphatics and valve-like folds of the mucosa which were situated at the uterine ostia of the tubes. In a few specimens not presenting these obstructions the gas entered the tubes at a pressure of 20 mm. Hg; the manometric fluctuations were uniform in rhythm and amplitude and averaged fifteen to the minute, a rate which was identical with the rate of muscle strip contractions during estrus.

During diestrus there was a marked irregularity in the character of the contractions; the two tubes from the same animal showed no similarity and the initial rise in pressure varied from 40 to 100 mm. Hg. There was no correspondence between the number of contractions as exhibited by isolated tube segments and by the intact tubes.

Uterotubal insufflation in the living monkey was undertaken by Morse and Rubin¹⁷ with the view of studying the relation between uterine and

*An abstract of this paper was presented at the International Congress of Obstetrics and Gynecology, May 6, 1938, at Amsterdam, Holland. The material contained therein was used in discussion of the paper by Geist, Salmon and Mintz on the "Effects of Estrogenic Hormone on the Fallopian Tubes," presented at the New York Obstetrical Society, October 12, 1937 and published in the issue of July, 1938 (page 67) of the JOURNAL.

tubal contractions and the menstrual ovulation cycle, and of establishing some graphic pattern which could be taken as evidence of ovulation. In respect to the latter, this work has reached only the preliminary stage, a method of approach being the first task to be accomplished. Intravenous injection of oxytocic and hormonal extracts have produced definite effects upon the intact uterus and tubes. The results so far obtained in the monkey have encouraged a similar clinical study.

Seekinger and Snyder⁷ were the first to study the cyclic changes in *extirpated human* Fallopian tubes by noting the contractions of isolated rings of muscle at various times of the menstrual cycle. They found that during the premenstrual phase the tubal contractions were of uniform amplitude but slower, about 4 per minute. More rapid contractions were found at the early interval stage while at the midinterval the contractions were rapidly increased in rate occurring at about 8 per minute and showing a striking variation in amplitude. In two of the latter showing 8 contractions per minute, it was possible for these observers to check the status of the ovary by laparotomy. In one case, an ovary showed a corpus luteum without signs of regression and in the other there was a recently collapsed follicle.

Intact temporarily surviving extirpated human Fallopian tubes also manifest rhythmic contractions when oxygen is insufflated through them, as I have had occasion to demonstrate a number of times. These motions are similar to those exhibited by living tubes in situ, a fact which was recognized in 1920 in the early experience with uterine insufflation. The human uterus, as far as we know, contains no anatomic structures at the tubal junctions resembling either the lymphatic apparatus or valve-like folds of mucous membrane which almost invariably hypertrophies at estrus in the lower animals that have been studied so far. This lymphatic apparatus offers a resistance to the passage of insufflated gases or injected fluids.

If ovulation in women is accompanied by definite changes in the rate of tubal contractions or other significant changes comparable to the results obtained in physiologic experiments on the isolated organs, it is conceivable that insufflation could serve as a method of identifying this event clinically. The search for a simple method appears to be all the more warranted because the only direct proof of ovulation is obtained by recovering ova from the Fallopian tubes as was done by Newell, Allen, Pratt and Bland.¹⁸ The time of ovulation can be approximately estimated by inspection of the corpus luteum. But as this requires a laparotomy, one is obliged to depend upon such indirect evidence as can be obtained by (1) histologic examination of the vaginal secretions; (2) endometrial biopsy and (3) biologic assays of the estrin content of blood and urine. Although time consuming, such quantitative determinations of estrogenic substances justify further efforts. Whether in conjunction with other criteria, which was recommended as desirable in 1928,¹⁹ or whether employed alone, it has seemed worth while to explore the possibility of using insufflation as another objective method of hormonal assay.

The routine performance of tubal insufflation as a test of tubal patency in women has brought out certain changes in the pattern of tubal contractions that appeared to me to bear a time relationship to the menstrual cycle. However, this impression was based upon random observations

in no definitely planned group of cases. In a paper published in 1928 on tubal patency it was stated that "there was not the same uniformity in the clinical cases which has been established by the muscle strip experiments in the lower animals." It was felt that "further observations along this line must be made in conjunction with parallel investigations that may be carried out in estimating the quantity of female sex hormone, etc. Whether the female sex hormone will prove responsible for activating the uterine mucosa and also tubal peristalsis at the same time, by increasing and decreasing quantities poured into the blood stream or through the follicle fluids directly into the oviduct remains to be determined."¹⁹

Though the parallel investigations suggested by me on the same group of patients whose tubal function was determined by insufflation were not undertaken, great strides were made in the estimation of estrogenic hormones.

The reasons for the random observations were twofold: (1) Since the primary object of insufflation was to test for tubal patency, the vast majority of patients were examined during the week following menstruation. (2) As the restoration of fertility was much desired, it was not deemed advisable to insufflate at other times of the menstrual cycle when the tubes might contain an impregnated ovum. Although the mechanical displacement of a tubal ovum may be regarded as hypothetical, the use of insufflation at other phases of the menstrual cycle was, nevertheless, limited prior to 1928 to those women who had had no coital relations for two weeks or more from the onset of the last regular menstruation. Additional data have been collated in the past ten years from a selected group of patients in whom for special reasons an insufflation was performed on days outside of the postmenstrual phase, their menstrual habit being regular and normal.

A fairly large group of patients whose menstruation was habitually delayed and a smaller group of cases of amenorrhea were available, serving the purpose of comparison. An analytical study was made of any striking variations in relation to the menstrual cycle which might be properly considered as characteristic of the ovulation phenomenon particularly and of ovarian function in general. A small number of menopausal cases and a larger group of artificial castrates were examined to get an idea of what degree of tubal function may be found when the ovaries are functionally or structurally ablated. In addition, a study has been made of a small group of women with frequent and profuse menses. In most instances the length of time consumed by the insufflation was from three to five minutes. In a smaller number the test was prolonged twice and three times. Several of the amenorrheic patients were treated with progynon injections and the effect upon the tubes as determined by insufflation was noted.

RESULTS

A. TUBAL CONTRACTIONS IN WOMEN WHOSE MENSTRUAL HABIT WAS REGULAR

There were in my series 100 women with normal tubal patency and normal menstrual cycles who were suitable for insufflation from the tenth to the sixteenth day of the cycle counting from the first day of the preceding menses. An equal number

were also insufflated from the sixteenth to the twenty-eighth day of the cycle. These two groups were compared to an equal number of a third group taken in sequence from the large series of patients tested for tubal patency between the seventh and the tenth day. The ages of the patients in the three groups were similar, from twenty to thirty-five years and the total number aggregated 300.

Several points were particularly noted during the insufflation:

1. *Initial Rise of Pressure.*—The pressure at which gas passed the uterotubal junction was taken to indicate uterotubal tone. In general, the patients who were insufflated during the tenth to the sixteenth day of the menstrual cycle required higher pressures, twice as often as the patients in the two other groups.

2. *Rate of Tubal Contractions.*—The number of contractions per minute was noted in the three groups. The contraction rate showed a tendency to be increased in the patients insufflated from the tenth to the sixteenth day of the cycle (Fig. 1). Thus 21 patients (21 per cent) of the tenth- to the sixteenth-day group had 7 to 9 contractions as compared to 8 patients (8 per cent) of the seventh- to tenth-day group, and 16 patients (16 per cent) of the sixteenth- to twenty-eighth-day group. The

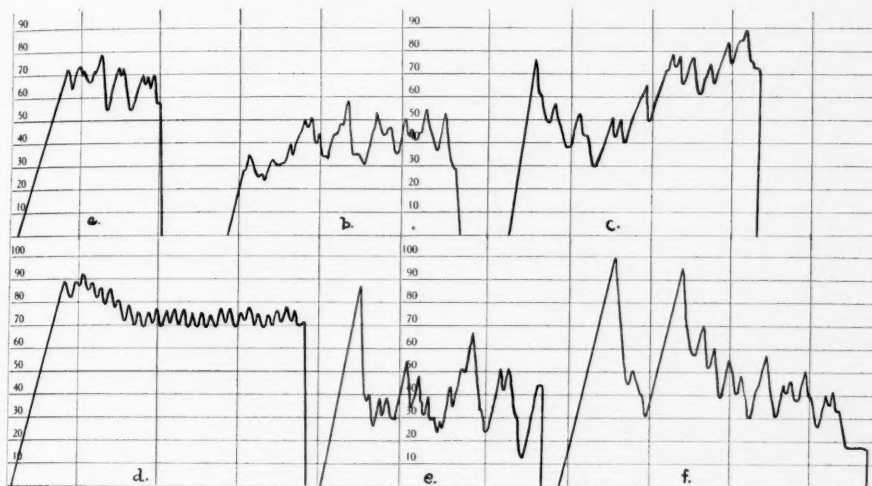


Fig. 1.—Insufflation at various intervals of the menstrual cycle: (a) Sixth day of cycle; (b) seventh day of cycle; (c) ninth day of cycle; (d) twelve day of cycle; (e) eighteenth day of cycle; (f) twenty-third day of cycle.

rest of the patients had less than 7 contractions per minute. In human tubes an increased contraction rate appears to be demonstrated during the period when ovulation is theoretically supposed to take place. On the other hand the presence of more frequent contractions during the other phases of the menstrual cycle suggest the possibility of ovulation taking place in women without the predictable regularity met with in lower animals. The overlapping in the three groups points to the possible shifting to a certain extent of the day of ovulation away from the fourteenth day.

3. *Amplitude of Tubal Contractions.*—The maximum range in amplitude of tubal contractions was noted in the three groups. The contractions ranged between 15 and 50 mm. Hg in 70 patients (70 per cent) of the seventh- to tenth-day group as compared to 71 (71 per cent) of the tenth to sixteenth-day group, and 73 (73 per cent) of the sixteenth- to twenty-eighth-day group. The remainder had maximum contractions of less than 15 mm. Hg. In many of the cases insufflated from the tenth to the sixteenth day of the cycle, shallow contractions were infrequent. Most of the fluctuations during this menstrual interval were of the maximum range and of perfect rhythm. In the two other menstrual phases contractions with the maximum range were few in comparison to the more shallow types.

B. TUBAL CONTRACTIONS IN WOMEN WITH HABITUALLY DELAYED, SCANTY OR ABSENT MENSES

Study of the possible hormonal influence upon the tubes was extended to instances of delayed menstrual periods in a group of women of the reproductive age. The patients studied had menstrual periods that were habitually delayed at least two weeks. Many had from 2 to 6 menstrual periods per year. Observations were made by means of insufflation and the kymograph upon tonicity, and upon the rate and amplitude of tubal contractions. Long-standing amenorrhea showed, in general, greater changes than did slight menstrual delay. No differences were noted between hypomenorrhea, oligomenorrhea, or hypo-oligomenorrhea.

There were 198 out of a series of 770 patients with habitually delayed periods who had normal tubal patency. As the kymograph was not used in 56 of these (early) cases, 142 remain of whom the findings can serve as a comparison with the normally menstruating group. The ages of the patients in the comparative groups were similar, ranging from 20 to 35 years.

Twenty patients had prolonged amenorrhea. In 9 of these the amenorrhea was of one or two years' duration; in 6 from 3 to 5 years; 2 of 6 years' duration; one patient had not menstruated for 8 years, and 2 patients for 14 years.

The remaining 122 patients were insufflated at the following intervals after their menses: in the first week 42; in the second week 32; in the third week 7; in the fourth week 7; in the second month 8; in the third month 11; in the fourth month 3; in the fifth month 2; in the sixth month 2; in the seventh month 4; in the eighth month 3; and in the ninth month 1.

The findings were as follows:

Initial Rise of Pressure.—The initial rise of pressure, i.e., the point at which the gas passed through the uterotubal junction, was strikingly lower in the patients of this group. Forty-four (30.9 per cent) had pressures between 20 and 50 mm. Hg as compared to 17 patients (11.9 per cent) of those with normal periods. Thirty-nine patients (27.5 per cent) of the group with hypo-ovarian function had pressures above 80 mm. Hg as compared to 45 patients (31.7 per cent) of those with normal periods. The rest of the patients had pressures between 50 and 80 mm. Hg.

Of the 20 patients with long periods of amenorrhea, 9 (45 per cent) had initial pressures under 50 mm. Hg; 10 (50 per cent) had pressures between 50 and 80 mm. Hg, and only 1 (5 per cent) had an initial pressure over 80 mm. Hg.

If the initial rise of pressure may be taken as an index of uterotubal tonicity, it would seem that it corresponds to the degree of ovarian hypofunction, i.e., the more pronounced the latter, the lower the uterotubal muscle tone.

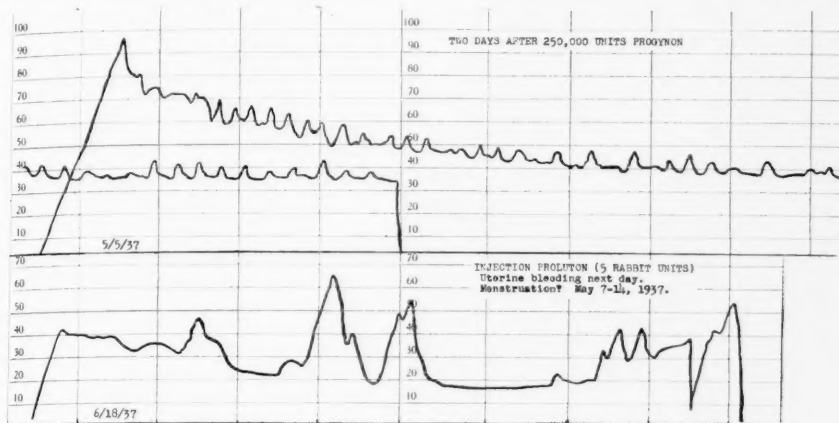
Contraction Rate.—There was a reduced contraction rate in the women with habitually delayed, scanty, and absent menses. Thus 92 cases (64.8 per cent) had 3 or less contractions per minute (7 had no tubal contractions) as compared to 31 cases (21.8 per cent) of the patients with normal periods. Only 12 patients (8.5 per cent) had more than six contractions per minute. This percentage was slightly less than that which obtained in the women with normal menstrual periods (12.7 per cent).

Exceptionally, hypertonicity was associated with amenorrhea. Whenever this was encountered it was felt that possibly the insufflation happened to be done at a phase of heightened follicle activity. Follow-up notes are lacking as to the occurrence of the next menstruation in these particular cases. The determination of the approximate time of ovulation in cases of habitually delayed menstruation, if feasible, would have the practical value of enabling us to predict the onset of labor in such cases with a greater degree of probability.

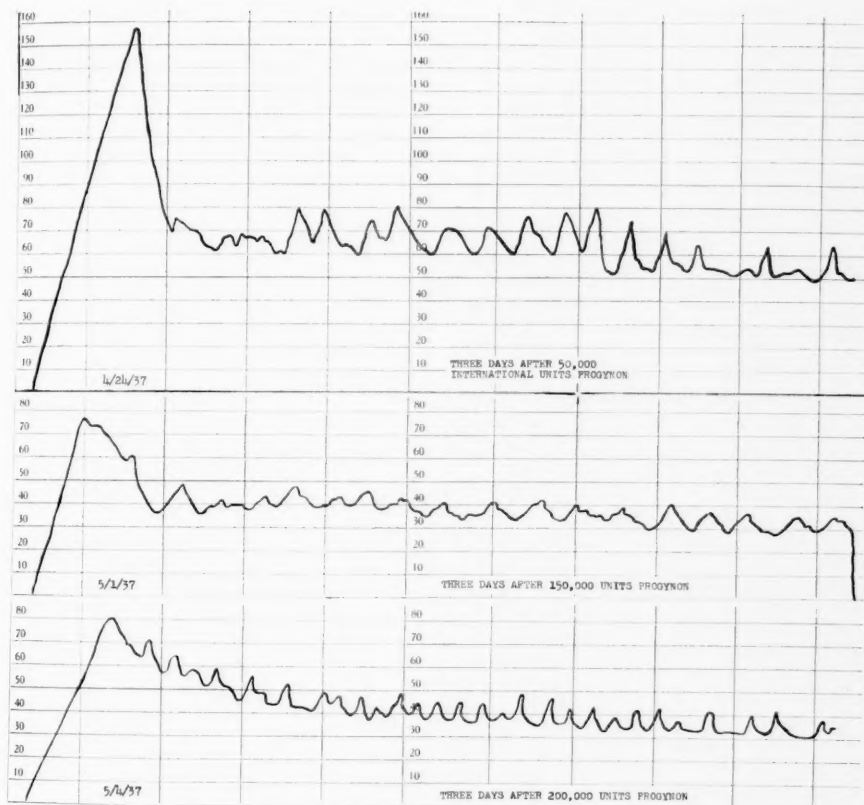
Judging from observations on the rate of contractions the latter appears to depend upon the degree of ovarian hypofunction. Thus of the 20 cases of long standing amenorrhea, 10 (50 per cent) had 3 or less contractions and only 2 (10 per cent) had 5 or more contractions per minute. These two cases may have been in or near the ovulation phase when the insufflation was done. One of the patients with an amenorrhea of fifteen months menstruated four months after the test, another with an amenorrhea of one year menstruated two months later. Two patients with amenorrhea of six to eight months menstruated within three weeks of the test. One other

having received large doses of progynon bled seven days after the injections were completed (Fig. 2, A, and B).

Range of the Contractions.—In the group of patients with scanty, delayed or absent menses, strong contractions were rare. Usually there were weak contractions



A.



B.

Fig. 2.—A and B, Effects of progynon injections on tubal contractions. Showing increased rhythmicity and higher uterotubal tonicity.

having an amplitude of 10 mm. Hg or less. Thus a frequent finding was one strong contraction to several weak contractions during an insufflation lasting three or more minutes.

Fatigability of the Tubes.—In 21 of the 142 cases with habitually delayed or absent periods, the tubes manifested fatigability by a decrease in the number and depth of contractions which occurred after a minute or two or longer (Fig. 3). Had the test been prolonged the incidence of fatigability might have been much higher. Fatigue occurred after one minute in 7 cases, after two minutes in 10 cases, after three minutes in 3 cases, and after four minutes in 1 case.

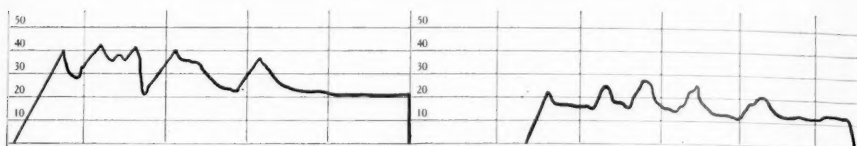


Fig. 3.—Graphs showing low initial pressures, poor tone, and fatigability as evidenced by loss of contractions after three minutes of insufflation.

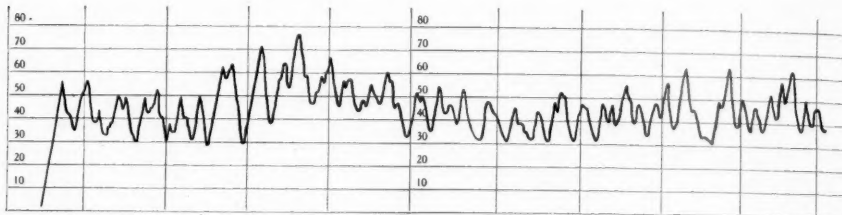


Fig. 4.—Rhythmic contractions in normal tubal patency with normal menstrual cycle. Note continuation of rhythmic contractions for ten minutes. This patient was insufflated for forty minutes in order to produce a large pneumoperitoneum. The contractions persisted throughout the insufflation.

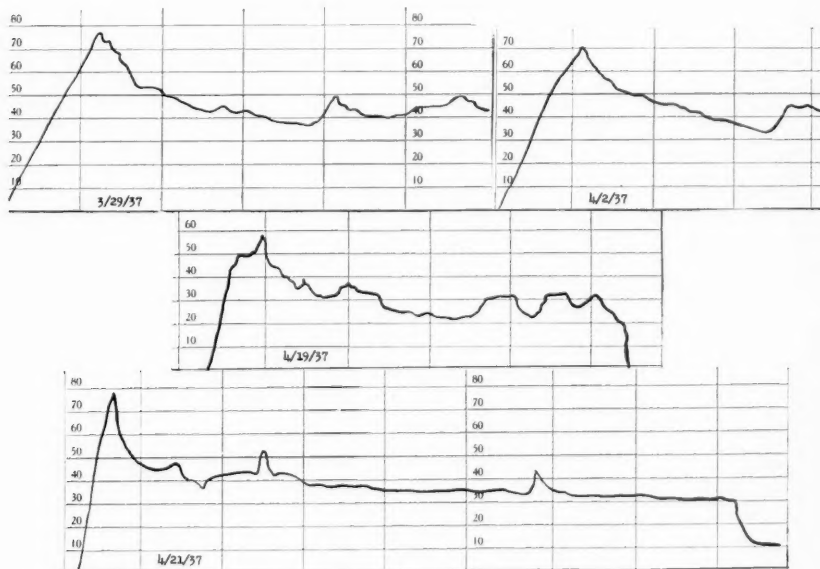


Fig. 5.—Insufflation at three day intervals in a patient with spontaneous secondary prolonged amenorrhea. Same patient as in Fig. 2, A and B.

This is a striking departure from the normal. In women with a normal habit of menstruation, the rhythmic contractions continue practically in a uniform way as long as the gas is permitted to flow through the tubes, at least for two to fifteen minutes (Fig. 4).

Cyclic Variation Demonstrated by Repeated Tests.—In 22 of the cases of amenorrhea, repeated tests were done, four at weekly intervals or oftener to note differences in the insufflation curve which might correspond to a cyclical pattern (Figs. 5 and 6). With the exception of two cases, the insufflation findings suggested such cyclical rhythm both with regard to the number of contractions per minute and the degree of tonicity. In one, the amenorrhea was of seven years' duration; insufflation was performed at weekly intervals. There appeared to be a cyclic change as demonstrated by a corresponding variation in the number, in the amplitude of contractions and to a less degree in the initial rise of pressure (tonicity).

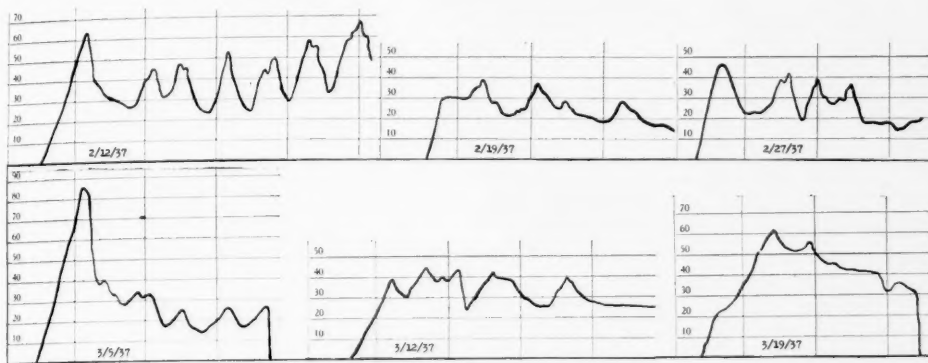


Fig. 6.—Insufflation at weekly intervals. Same patient as in Fig. 2, A and B.

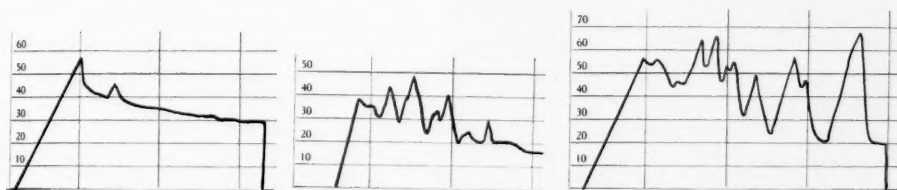


Fig. 7.

Fig. 8.

Fig. 9.

Fig. 7.—Insufflation of patient 55 years old; menopause of nine years' duration. Note absence of tubal contractions.

Fig. 8.—Insufflation of patient following x-ray abortion (castration dose). Graph shows a low pressure level and tendency to fatigability (absence of contractions) after two minutes.

Fig. 9.—Patient with menorrhagia insufflated at seventeenth day of cycle. Note deep strong tubal contractions.

Tubal Contractions in the Menopause.—Insufflation was performed in 9 women at the menopause, ranging in age from 40 to 49, in whom menstruation had ceased from three months to nine years. In all 9 there were a low initial pressure rise and infrequent shallow or absent fluctuations (Fig. 7). The initial rise of pressure at which the gas passed the uterotubal junction varied from 25 mm. Hg to 80 mm. Hg; 5 of the patients having an initial pressure rise below 50 mm. Hg. In 4 patients there were no tubal contractions whatever; in the remainder the contractions were infrequent and rarely reached a depth above 5 mm. Hg. The uniformity of these findings would appear to correspond with the lowered or absent hormonal output of the ovaries during the menopause. It need only be mentioned that deductions can be made only when the tubes are freely patent; when obstructed the initial pressure is, naturally, high.

Effect of "Stimulating" Doses of X-ray and Radium on Tubal Contractions.—In five cases with delayed periods (ovarian hypofunction), the tubes were insufflated both before and after treatment with "stimulating" doses of x-ray or radium. There was no appreciable effect upon the initial rise of pressure. In all 5 there was an increase in the contraction rate. Of 2 patients who exhibited no contractions before x-ray stimulation, one had 3 contractions after treatment and the other 5 contractions per minute. The depth of contractions was also increased; in one to a range of 5 to 20 mm. Hg and in the other it fluctuated round about 5 mm. Hg.

Effect of X-ray Castration on the Tubes (Dosage for the Induction of Abortion).—The effect of x-ray castration on the tubes was studied in 33 women who had had a therapeutic abortion by x-ray. As these women were all still in the reproductive period, their tubes being normal, they afforded an exceptional opportunity to study the contraction curves as determined by uterotubal insufflation (Fig. 8).

Twenty-two patients, or 66.6 per cent of the group, had initial pressure rises under 50 mm. Hg, as compared to 11.9 per cent of patients with a normal menstrual cycle. Only 2, or 6.1 per cent, had pressures above 80 mm. Hg, as compared to 31.7 per cent of the group with normal menstrual cycle. Nine patients, or 27.3 per cent, had pressures from 50 to 80 mm. Hg.

An actual increase in the number of contractions was seen at the onset of the insufflation in a third of this group. But after the first minute or two the oscillations were only occasional, or altogether absent showing definite signs of fatigue. Moreover, though they were occasionally as well marked as in cases with normal menstrual function the weaker contractions were generally more conspicuous.

C. TUBAL CONTRACTIONS IN WOMEN WITH FREQUENT AND PROFUSE MENSES

A further study of the possible hormonal influence upon the tubes was made in a group of 29 women with profuse and frequent periods. In a group of 156 cases of sterility associated with profuse and frequent periods only these 29 (18.6 per cent) had normal tubal patency (Fig. 9).

Initial Rise of Pressure.—The point at which the gas passed through the uterotubal junction, was markedly higher in the patients of this group. Only 1 (3.4 per cent) had a pressure below 50 mm. Hg as compared to 30.9 per cent of the larger group with delayed and scanty periods, and 11.9 per cent of those with normal periods. Nineteen (65.5 per cent) of the group with frequent and profuse periods had initial pressures above 80 mm. Hg as compared to 27.5 per cent of the group with hypovarian function and 31.7 per cent of those with normal periods. The rest of the group had pressures between 50 and 80 mm. Hg.

These findings would seem further to substantiate the belief that the tonicity and initial pressure are proportional to the degree of ovarian function.

Contraction Rate.—The contraction rate in women with profuse and frequent menses maintained a midway course between the group of women with delayed and scanty periods and those with normal menses. Thus, 29 (44.4 per cent) had 3 or less contractions as compared to 64.8 per cent of the group with delayed and scanty periods and 21.8 per cent of the patients with normal periods. Only 1 (3.4 per cent) had more than six contractions.

Range of the Contractions.—The range of contractions in women with frequent and profuse periods was less than that of women with normal periods, and exceeded that of women who had habitually delayed and scanty periods. Thus, 18 (62.1 per cent) had contractions with a range of 15 to 50 mm. Hg as compared to 71.3 per cent of the patients with normal periods, and the rare case in the group with delayed and scanty periods. The remaining 11 cases (37.9 per cent) had contractions under 15 mm. Hg.

SUMMARY

The character of tubal contractions as elicited by uterotubal insufflation was studied in relation to the type of menstruation in 513 patients with tubal patency. The patients with normal menstruation were

divided into three groups: (1) those who were insufflated from the seventh to the tenth day, counting from the first day of the menses; (2) those between the tenth and sixteenth days, and (3) those between the sixteenth and twenty-eighth days. Because of the greatest interest in identifying the event of ovulation, which is said to occur between the tenth and sixteenth day of the menstrual cycle, more than half of the cases fell into Group 2, totaling 300. These three groups were compared to each other and also served as a comparison for patients with abnormal menstrual cycles.

There were 142 patients with habitually delayed menses, 20 with prolonged spontaneous amenorrhea, and 33 who had been subjected to x-ray castration for the purpose of inducing abortion. There were 5 women in this series who had been subjected to treatment by so-called stimulating doses of x-rays to regulate the menses. Nine women who had entered the menopause had their tubes insufflated for comparative purposes. In addition, tubal contractions were studied in a group of 20 women with frequent and profuse periods.

The results of this study have shown that:

A. In general the tubes in patients with normal menstrual cycles exhibit during insufflation uniform contractions and relaxations varying in rate between 3:4 to 8:9 per minute; the less frequent rate coinciding with the anovulation phase (7:10 and 16:28 days); the more frequent rate of contractions with the ovulation phase (10:16 days). The tonicity of the tubes is moreover somewhat greater during the ovulation phase as evidenced by deeper ranges of pressure fluctuations.

B. In the patients with habitually delayed menses the uterotubal tone is in general lowered and the contraction relaxation rate less frequent per minute except when insufflation happens as it appears to coincide with a possible ovulation phase.

C. In the group of cases of spontaneous prolonged amenorrhea occurring during the reproductive period, uterotubal tone, frequency and range of tubal contractions are as a rule decreased, although a cyclical variation may be demonstrated in a number of them. In the amenorrhea of menopause, uterotubal tone, contraction rate and amplitude are all markedly diminished, contractions being frequently absent.

D. In x-ray castration during the reproductive period, a certain cyclical pattern is frequently maintained but the tonicity and frequency of contractions are relatively diminished.

In the cases where so-called stimulating doses of x-ray were used, the effects upon the contraction rate and amplitude are augmented.

E. In the cases of frequent and prolonged menses, uterotubal tone, contraction rate and amplitude are less than in patients with normal periods and more than the group with habitually delayed and scanty menses.

There appears to be a definite correlation between the character of tubal contractions as elicited by tubal insufflation and the menstrual function. Since the menses depend in the main upon ovarian function, whether this be primary or subordinated to the pituitary or other inner secretory glands, it follows that absence of menses or depressed menses

may be assumed to be due to under-function of the ovaries. As tubal contractions are influenced by the hormonal action of the ovaries, any deviation from the normal may therefore be reflected in the pattern of tubal contractions. This appears to be susceptible of clinical assay and demonstration by uterotubal insufflation. In a few cases of prolonged secondary amenorrhea systematic injection of progynon was carried out. A dynamic effect upon the tubes appeared to be demonstrated (note Fig. 2). Where there had been shallow or irregular and infrequent contractions prior to the progynon injections, they became regular, of increased amplitude and frequency after the injection.

In order to establish typical patterns corresponding to the ovulation phase, a greater number of cases will have to be examined by this method and paralleled by blood and urine estrogen determinations as well as histologic examination of uterine and vaginal biopsies. The method is limited to patients with normally patent Fallopian tubes. When the tubes are nonpatent the uterus may serve as the medium for this assay by the same method.*

REFERENCES

- (1) *Rubin, I. C.*: AM. J. OBST. & GYNEC. **14**: 557, 1927. (2) *Kehrer, E.*: Arch. f. Gynäk. **81**: 160, 1907. (3) *Blair, E. W.*: Proc. Am. Assn. Anat. Rec. **23**: 9, 1922. (4) *Corner, G. W.*: Am. J. Anat. **32**: 345, 1923. (5) *Frank, R. T.*: The Female Sex Hormone, Springfield, Ill., 1929, Charles C. Thomas. (6) *Reynolds, S. R. M.*: Physiol. Rev. **17**: 304, 1937. (7) *Seckinger, D. L., and Snyder, F. F.*: Johns Hopkins Hosp. Bull. **39**: 371, 1926. (8) *Wislocki, G. B., and Guttmacher, A. E.*: Johns Hopkins Hosp. Bull. **35**: 246, 1924. (9) *Westman, A.*: Acta obst. et gynec. Scandinav. **10**: 288, 1930. (10) *Manzi, L.*: Arch. di. ostet. e. ginee. **38**: 591, 1931. (11) *Moir, C.*: Trans. Edinburgh Obst. Soc. **190**: 93, 1933-1934. (12) *Andersen, D. H.*: Am. J. Anat. **42**: 255, 1928. (13) *Moreau, R.*: Arch. d'anat. Micr. **14**: 315, 1913. (14) *Lee, F. C.*: Bull. Johns Hopkins Hosp. **42**: 355, 1928. (15) *Mikulicz-Radecki, F.*: Zentralbl. f. Gynäk. **54**: 2183, 1930. (16) *Whitelaw, M. J.*: AM. J. OBST. & GYNEC. **25**: 475, 1933. (17) *Morse, A. H., and Rubin, I. C.*: AM. J. OBST. & GYNEC. **33**: 1087, 1937. (18) *Newell, Q. U., Allen, E., Pratt, J. P., and Bland, L. S.*: AM. J. OBST. & GYNEC. **19**: 180, 1930. (19) *Rubin, I. C.*: J. A. M. A. **90**: 90, 1928.

*Although easily carried out, as has been demonstrated a number of times in the female monkey and in women, my work has not progressed far enough to warrant deductions. It may only be noted that it can serve satisfactorily and is simple to carry out.

ROLE OF THE UTERUS IN THE PRODUCTION OF MANOMETRIC FLUCTUATIONS DURING UTEROTUBAL INSUFFLATION (RUBIN TEST)*

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SINCE Kehr¹'s classic experiments with isolated strips of excised tube, numerous animal experiments have demonstrated the presence of tubal contractions and peristalsis. In May, 1925, Rubin² began the study of human tubal peristalsis by recording on a revolving drum the variations in pressure coincident with the passage of gas through the uterus and tubes.

Guthman³ was the first to express the opinion that manometric fluctuations were due to tubal peristalsis. He based this conclusion on the well-known fact that when the tubes are closed, fluctuations are not observed on the manometer. Much experimental work was done to substantiate this contention. However, further evidence is necessary to determine whether or not the uterus participates in the production of manometric fluctuations during uterotubal insufflation, and if so, to what extent. To clarify this subject, these experiments have been carried out on the uterus and tubes of living rabbits, and on excised specimens.

MATERIAL AND METHOD

Experimental observations were made on the intact uteri and tubes of 60 mature rabbits, weighing from 2 to 4 kilograms. They were anesthetized by the intravenous injection of nembutal, 1 gr. to 2.2 kilograms. Further studies were made on the excised specimens suspended in oxygenated Locke solution.

Changes in manometric fluctuations during gas insufflation of the uterus and tubes were recorded on the kymograph of the Rubin apparatus.⁴ Carbon dioxide gas under 15 pounds of pressure was employed at a constant rate of flow, one second being required for the passage of 1 c.c.

For the routine uterotubal insufflation, a bulb tipped medicine dropper or Keyes-Ultzman cannula was passed into the uterus through a small incision 2 cm. from the uterotubal junction, and tied tightly. For retrograde tubouterine insufflation, a needle cannula was tied in the fimbriated end of the tube. For uterine insufflation alone, the cannula was tied into a segment of uterus, the wall of which was punctured to allow the gas to escape through it and thus preventing it from passing through the uterotubal junction and tubes. For tubal insufflation alone, a needle cannula was passed through the uterotubal junction into the tube, and tied tightly.

In order to demonstrate focal contractions of the uterine and tubal muscle a small needle hook was passed through the entire thickness of muscle, down to the mucosa, and the contractions were recorded on a smoked drum.

TUBAL PATENCY NECESSARY FOR MANOMETRIC FLUCTUATIONS

During uterotubal insufflation, pressures of 50 to 200 mm. Hg were necessary in different rabbits to force the gas from the much wider uterine cavity through

*We are indebted to Dr. I. C. Rubin for the suggestion and supervision of these experiments.

the narrow uterotubal junction. Once the gas passed this narrow aperture, there was a drop in pressure and manometric fluctuations were recorded as long as the gas was allowed to pass through the tubes.

In 10 experiments in which gas failed to pass the uterotubal junction at pressures of 200 to 220 mm. Hg, there were no pressure fluctuations. In three experiments the tubes were patent to the gas and exhibited pressure oscillations as the gas flowed through them. When these tubes were clamped off the fluctuations ceased. When the pressure was released 10 mm. Hg at a time by means of a release valve down to the lowest pressure levels, no fluctuations were produced. However, when the clamps were removed from the tubes of these three rabbits, manometric oscillations appeared with visible peristalsis of the tubes. The pressure patterns were somewhat altered at first owing to the momentary injury, but they rapidly regained their previous undisturbed character.

Whenever the intrauterine pressure was below that which was required for the gas to pass the uterotubal junction, no manometric fluctuations occurred.

These experiments indicate that tubal patency must be present for the demonstration of manometric fluctuations during uterotubal insufflation.

COMPARISON OF INSUFFLATION OF THE UTERUS ALONE WITH UTEROTUBAL INSUFFLATION

In the undisturbed state the uterus and Fallopian tubes were seen to undergo rhythmic peristaltic movements. However, during uterotubal insufflation, the uterus

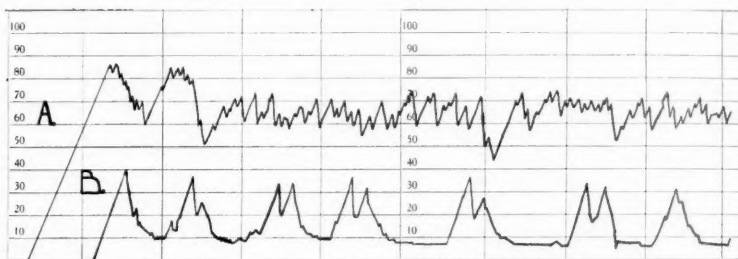


Fig. 1.—A, Uterotubal gas insufflation, showing numerous manometric fluctuations. B, Insufflation of solitary uterine segment, showing fewer and deeper manometric fluctuations at a lower pressure level.

became distended and remained so as long as the gas was allowed to pass through the tubes. This distended organ appeared inactive. Occasionally, as was noted in three rabbits, the gas passed the uterotubal junction at a low pressure without causing marked distention of the uterus, and weak uterine peristaltic movements were noted. Once distended, the uterus was found to lose its contractility temporarily, so that for comparison with uterotubal insufflation, a segment of uterus was insufflated which had not been subjected to previous distention. A segment of uterus 5 cm. in length was employed for this experiment, the tube being entirely excluded. Gas was allowed to escape through a small opening made in the uterine wall. The direction of the cannula in the uterus, toward or away from the vagina, had little effect on the findings.

In the phase of contraction the uterus or tube became shorter and thicker. During insufflation, the contractions appeared simultaneous with the upward rise of the mercury pressure and the upward stroke on the drum. During relaxation the pressure dropped. During the contraction gas would either fail to escape from the fimbria or the small opening in the uterus, or when it did pass through these points it came out in the gentlest stream of small bubbles. The moment the contraction ceased (relaxation phase) the gas at once escaped in large, rapidly succeeding bubbles.

In 30 experiments the contractions obtained by insufflating a solitary segment of uterus were entirely different from those of uterotubal insufflation (Fig. 1). The uterotubal junction acted as a barrier to the gas to a pressure far in excess to that which was necessary when the gas passed through the uterine opening. Thus, gas passed through the artificial uterine opening at pressures of 10 to 50 mm. Hg. The pressures required to force gas through the uterotubal junction to record tubal contractions varied from 50 to 200 mm. Hg, and correspondingly higher pressure levels were maintained as long as the gas was allowed to flow. When the uterus alone was insufflated, the rate of contractions was much less than when the tube was included.

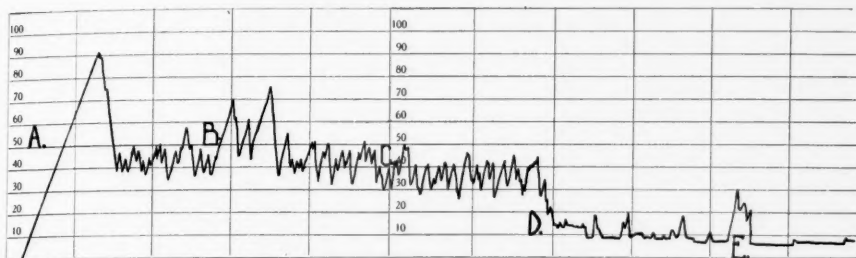


Fig. 2.—A, Uterotubal gas insufflation. B, Insufflation after excision of half of ampulla. C, Insufflation after excision of entire ampulla. D, Insufflation after excision of half of isthmus, showing an occasional shallow contraction. E, Insufflation after excision of entire isthmus. Note absence of manometric fluctuations.

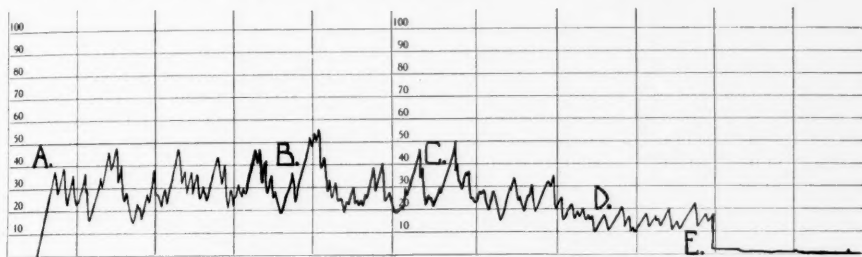


Fig. 3.—A, Tubouterine gas insufflation. B, Insufflation after excision of uterus. C, Insufflation after excision of tubouterine junction. D, Insufflation after excision of half of isthmus. E, Insufflation after excision of entire isthmus. Contractions have disappeared.

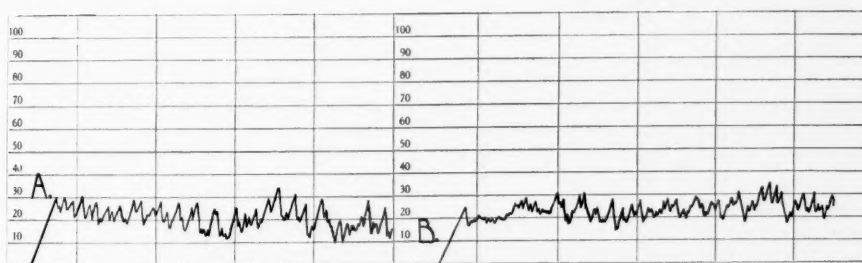


Fig. 4.—A, Uterotubal gas insufflation. B, Insufflation of tube (uterus excluded). Note similarity of manometric fluctuations recorded.

In 12 tests there were less than 4 contractions per minute; during uterotubal insufflation there were always more than 4 contractions per minute. In 14 experiments uterotubal insufflation registered 10 to 16 contractions per minute; when the uterus alone was insufflated there were never more than 9 contractions per minute. The uterine contractions usually had a larger amplitude than those which were obtained at uterotubal insufflation. When the uterus alone was insufflated, there were

only 9 tests with contractions of an amplitude less than 15 mm. Hg, the others having a range of 15 to 50 mm. Hg. During uterotubal insufflation there were 24 tests in which the contractions had an amplitude less than 15 mm. Hg, and only 6 with a depth of 15 to 30 mm. Hg.

EFFECT OF EXCISING SEGMENTS OF TUBE AND UTERUS, AND UTEROTUBAL JUNCTION

During nine uterotubal insufflations successive segments of tube from the fimbria toward the uterus were excised, eventually cutting off the uterotubal junction. Usually, a momentary rise in pressure resulted from the excision. However, after a minute or less the contractions regained their usual pattern.

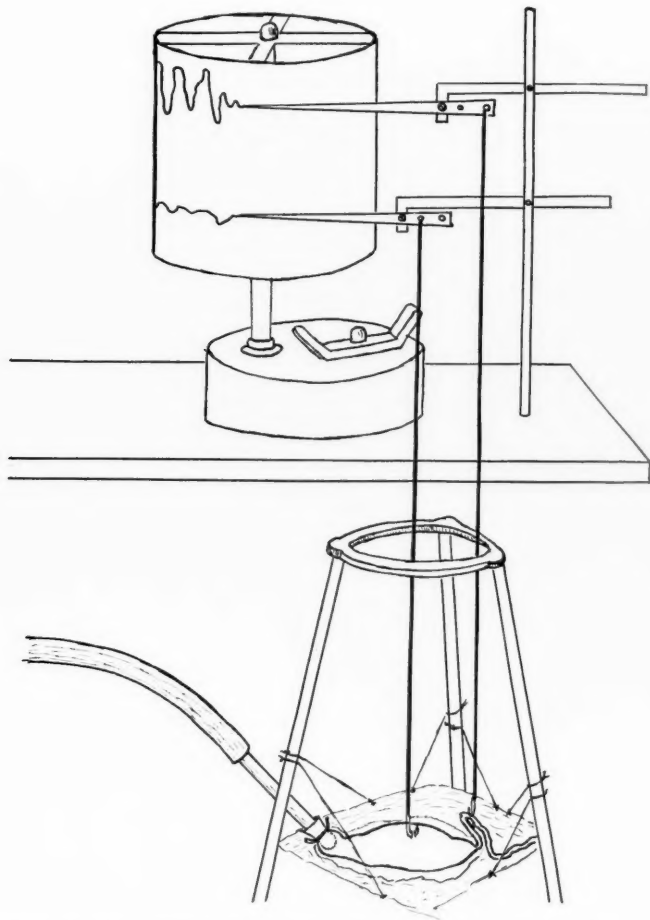


Fig. 5.—Sketch showing uterine and tubal muscle lever preparation with cannula for gas insufflation leading to the Rubin apparatus.

Excision of the outer third of the tube did not affect the character of the contractions. Excision of the entire ampulla, leaving the isthmus, did not affect the depth of contractions, but in one-third of the tests the contractions were slightly less frequent and were maintained at a lower pressure level. When only half of the isthmus remained, the contractions were rare and at a much lower pressure level.

As long as any portion of the tube remained, manometric fluctuations were recorded on the kymograph.

In four tests in which gas had passed the uterotubal junction at pressures below 50 mm. Hg, the uterus was not distended and muscle tone was retained. The result was an occasional weak manometric fluctuation from the uterus when the entire tube and uterotubal junction were excised. In five tests which required high pressures so that the uterus was markedly distended during uterotubal insufflation, no contractions occurred when the tube and uterotubal junction were excised (Fig. 2).

In ten experiments tubouterine insufflation was performed through a needle cannula, tied in the fimbriated end of the tube. When the entire uterus was excised up to the uterotubal junction, no change was noted in the manometric fluctuations. Excision of the uterotubal junction merely resulted in a slight lowering of the base line at which the manometric changes occurred. Excision of half of the isthmus



Fig. 6.—A, Contractions registered by hook in tubal muscle. B, Contractions registered by hook in uterine muscle. A₁, Contractions registered by hook in tubal muscle during uterotubal insufflation, showing no alteration in strength. B₁, Contractions registered by hook in uterine muscle during uterotubal insufflation, showing diminished muscle action. C, Contractions registered by uterotubal gas insufflation on the kymograph of the Rubin apparatus during the recording of A₁ and B₁.

did not affect the depth of contractions. In three tests, there were 2 to 3 contractions more per minute. There was a drop of 10 to 30 mm. Hg in the pressure level at which the gas maintained itself. When all of the isthmus was excised, gas bubbled through the ampulla almost continuously at a level of 0 to 8 mm. Hg, with the production of an occasional weak manometric fluctuation (Fig. 3).

From the above experiments, it appears that the uterus exhibits contractions during uterotubal insufflation only when it is not distended.

Excision of successive segments of the Fallopian tube indicates that the ampulla has very little power of contractility, and that this property is relegated to the more muscular isthmus.

COMPARISON OF UTEROTUBAL AND TUBAL INSUFFLATION

In six experiments, an opportunity was afforded to compare the pressure changes recorded by uterotubal insufflation with those obtained by insufflating the tube alone. Following uterotubal insufflation, a needle cannula was passed through the uterotubal junction and pressure changes were recorded during insufflation of the tube itself.

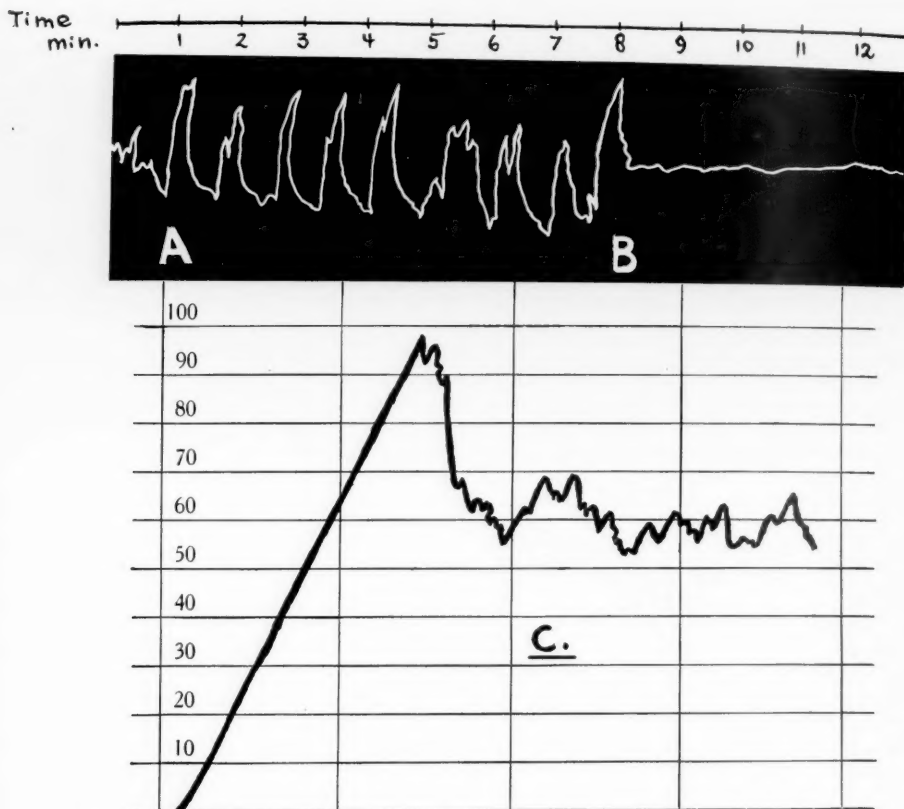


Fig. 7.—A, Contractions registered by hook in uterine muscle. B, Uterotubal gas insufflation was performed, resulting in an absence of uterine muscle function. C, Manometric fluctuations recorded on the kymograph of the Rubin apparatus, corresponding to the recording of B.

The manometric fluctuations obtained during uterotubal and tubal insufflation were similar. There was no noticeable difference in the contraction rate. During uterotubal insufflation the contractions were occasionally deeper, and higher pressures were required to force gas through the narrower uterotubal junction (Fig. 4).

CONTRACTION STRENGTH OF UTERINE AND TUBAL MUSCLE DURING UTEROTUBAL INSUFFLATION

The contraction strength of uterine and tubal muscle during uterotubal insufflation was determined in five rabbits *in vivo* by placing a hook in the uterine

muscle and another in the tubal muscle, and registering muscle action of both simultaneously on a smoked drum. Before insufflation, strong contractions of both the uterine and tubal muscle were seen. During uterotubal insufflation, the tubal muscle action was unaltered. The uterine muscle contractions nearly disappeared in 3 experiments and were absent in 2 others (Figs. 5 and 6).

In five other experiments, a solitary needle hook was placed through the uterine muscle and recordings made on a smoked drum before and during uterotubal insufflation. Before insufflation, large uterine contractions were observed. During insufflation, a rare contraction occurred in three instances and none were noted in two experiments (Fig. 7).

To eliminate the effect of extraneous factors such as intestinal and respiratory movements, these experiments were repeated on the excised uterus and tubes of seven rabbits, suspended in oxygenated Locke solution. No effect was noted on tubal muscle function during uterotubal insufflation. In the undisturbed state strong uterine muscle contractions were recorded on the smoked drum. However, when the uterus became distended by the insufflated gas, muscle contractions were rare or entirely absent.

In the above experiments, the hook on the uterus did not cause any change in the manometric fluctuations recorded on the kymograph of the Rubin apparatus during uterotubal insufflation. Only when the hook in the tubal muscle prevented free movement of the tube, did the manometric fluctuation become weaker, irregular, or absent. Similar results were observed when the uterus and tube were alternately fixed to the abdominal wall by sutures.

From the above observations, it appears that distention of the uterus as produced by uterotubal insufflation, results in a diminished or absent function of the uterine muscle. The tube, on the other hand, shows no visible distention and its muscle function remains unaltered. The diminished or absent muscle action of the uterus, when insufflated, would limit its participation in the production of manometric fluctuations during uterotubal gas insufflation.

SUMMARY

Experimental observations were made on the uteri and tubes of 60 living rabbits to determine whether or not the uterus participates in the production of manometric fluctuations, which are uniformly seen during uterotubal gas insufflation.

Manometric fluctuations occurred during uterotubal insufflation only when tubal patency was present.

The undisturbed uterus and tubes were seen to undergo rhythmic peristaltic movements. During uterotubal insufflation the uterus became distended and its motion was reduced or disappeared. The tube, on the other hand, showed no visible distention and its motion was unaltered.

The character of the contractions obtained by insufflating a solitary uterus was entirely different from the pattern recorded during uterotubal insufflation.

Excision of successive segments of the tube during uterotubal or tubouterine insufflation showed that the ampulla has very little power of contractility, and that this property is possessed by the more muscular isthmus. During tubouterine insufflation, excision of the uterus had no effect on the production of manometric fluctuations.

When the tube alone was insufflated, there was no noticeable difference in the character of the contractions obtained with the uterus

excluded, showing definitely that the latter did not have any influence in the production of the contraction waves as demonstrated on the kymograph of the Rubin apparatus.

Recording uterine and tubal muscle function during uterotubal insufflation by means of delicate hooks in the muscle attached to writing levers on a smoked drum, revealed that distention of the uterus resulted in a diminished or complete absence of function. The patent tube, on the other hand, does not become overdistended by any pressure levels during gas insufflation, and its muscle function remains unimpaired.

CONCLUSION

Experiments on rabbits indicate the limited degree to which the kymographic curves of pressure fluctuations (rhythmic contractions) observable during uterotubal insufflation are influenced by the uterine muscle, and that therefore these manometric fluctuations are due to the unimpeded action of tubal muscle in freely patent tubes.

REFERENCES

- (1) *Kehrer, E.*: Arch. f. Gynäk. **81**: 160, 1907. (2) *Rubin, I. C.*: AM. J. OBST. & GYNEC. **14**: 557, 1927. (3) *Guthman, H.*: Monatschr. f. Geburtsh. u. Gynäk. **69**: 10, 1922. (4) *Rubin, I. C.*: J. A. M. A. **92**: 1597, 1929.

PREGNANCY WITH LEUCEMIA*

A CASE REPORT AND REVIEW OF THE LITERATURE

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A YEAR ago the authors saw a woman with acute lymphatic leucemia, which became apparent in the fifth month of her second pregnancy. This case is herewith reported:

Mrs. C. B. D., aged 29 years, was cared for by one of us in 1935 through her first pregnancy which was uneventful. The Wassermann was negative and blood findings were normal. The baby is alive and well.

Her past history was entirely normal except for the usual childhood diseases. Her tonsils had been removed. Menstruation had always been normal. A chronic ear infection had persisted for years.

She came under observation for this pregnancy on March 20, 1937. Her last menstrual period was Dec. 5, 1936. No abnormal findings were noted. The hemoglobin was 81 per cent and the erythrocytes 4,120,000. There were no unusual complaints until May 12, 1937, when she developed headache, malaise, frequent stools, and a low grade fever. These symptoms disappeared in a few days on rest in bed, a liquid diet, and a few doses of paregoric. However, on May 22, they returned and she noticed in addition, petechiae on the arms and legs, enlargement of the cervical glands and bleeding from the gums. A blood examination was made at this time which revealed: hemoglobin 48 per cent, erythrocytes 2,250,000, leucocytes 295,000 with 97 per cent lymphoblasts. The platelet count was 93,000. Hospitalization was advised but refused. She remained in bed until entering the hospital on May 30.

*Presented at the meeting of the Chicago Gynecological Society, May 20, 1938.

A physical examination on admission showed in addition to the above findings: no petechiae in the eyes or mouth; a normal tongue and marked adenopathy of the occipital and axillary nodes. Only the cervical nodes were tender. There was no enlargement of the heart but a slight systolic murmur was heard at the apex. The lungs were clear. There were numerous areas of hemorrhage under the skin from previous minor bruises of the extremities. The liver and spleen were palpable two fingerbreadths below the costal margins. The fundus of the uterus was at the level of the umbilicus. A blood smear showed almost exclusively lymphoblasts. The coagulation and bleeding times were abnormally long.

A diagnosis of acute lymphatic leucemia was made. Interruption of the pregnancy was considered inadvisable at this time because of the danger of hemorrhage and the child was not viable. Blood transfusions were given four times in the next eight days because of the anemia. There was some improvement in the hemoglobin and the number of red cells but very little reduction in the lymphoblasts. The patient felt a little subjective improvement. The size of the liver and spleen was slightly reduced. The patient wanted to go home. X-ray therapy was decided upon and 50 r. were given over the entire body excluding the uterus. She went home the same day, June 9, 1937.

Three days later she returned with severe pain in the left hypochondrium. The abdomen was distended with flatus and by the greater enlargement of the liver, spleen, and uterus. An enema gave some relief. There was marked bleeding from the nose and swollen lips and gums. The nodes previously mentioned were much larger and the inguinal nodes were now tender and palpable. The next day she complained of red spots before her eyes.

All these symptoms and findings increased in severity. On June 17 blood appeared in the urine and occult blood was found in the stools. Because of a decrease in the hemoglobin and erythrocytes another transfusion of 500 c.c. of citrated blood was given. After the x-ray therapy there was a decided reduction in the number of lymphoblasts. By the twenty-second of June there was another rise and so she was given a second treatment with x-ray. Again a reduction was noticed in the lymphoblasts, but the patient's condition appeared to be worse.

The next day about 4:00 P.M. painful uterine contractions began. After receiving one international unit of proluton these subsided until 9:00 P.M. when labor was again definitely in progress. She had been irrational for several hours. Her temperature was 102° F. By 10:00 P.M. the cervix was dilated to 4 cm. Morphine gave some relief from pain. At 11:30 P.M. 20 c.c. of thromboplastin was given intravenously because of fear of hemorrhage with delivery. At 2:30 A.M. on the twenty-third of June the dilatation of the cervix was 5 to 6 cm. and the membranes were ruptured artificially. At 3:15 A.M. a living male fetus was delivered spontaneously in frank breech presentation after six and a quarter hours of labor. There was moderate bleeding during labor. The placenta was easily expressed. The uterus contracted well, but moderate bleeding continued. It was packed with eight yards of gauze. About 400 c.c. of blood was lost. She was immediately given 300 c.c. of normal saline and 300 c.c. of citrated blood by transfusion. On leaving the delivery room, the patient's pulse was 140, and the blood pressure was 90/72. By 9:00 A.M. her pulse was 100 and the temperature 98.6° F. She felt better than she had for several days. At 10:15 A.M. 400 c.c. more of blood was given. By 4:00 P.M. her temperature was 104.4° F., pulse 120, and respirations 26. The uterus was no longer firm and bleeding through the pack began in spite of the use of ergotrate. At 6:30 P.M. the pack was removed followed by several large clots.

The patient was unconscious and in such extreme condition that it seemed useless to repack. At 7:30 P.M. 20 c.c. more of thromboplastin were given. By 11:30 P.M. copious involuntary bloody stools were repeatedly passed and uterine hemorrhage continued. The patient died at 6:05 A.M. on June 24, twenty-seven hours after delivery and forty-three days after the appearance of her first subjective symptoms of leucemia. This was thirty-three days after the diagnosis was confirmed by complete blood examination. The baby lived for six hours. It weighed 1,280 gm. The autopsy showed no evidence of leucemia in the baby. A blood examination before death was as follows: hemoglobin 12.5 gm., 81.8 per cent; red blood cells 3,870,000,

TABLE I. TEMP.—HEMATOLOGY—THERAPY

1937	MAY 30	JUNE 1	JUNE 9	JUNE 12	JUNE 17	JUNE 22	JUNE 23
Temp.	100.2	100.4	98.4	99.8	100	102.2	105.8
Pulse	106	106	90	128	106	126	140
Hb. gm.	—	7.5	10.5	10	6	5.5	6
Hb. %	48	48.7	68.1	64.9	39	37.7	38.9
R.B.C.							
Millions	2.45	3.02	3.78	3.41	2.49	2.82	2.66
W.B.C.							
Thousands	295	410	265	124	48	75	48
Platelets		78,520			43,200	36,480	
Transfusions	4 times—500 c.c.				500 c.c.		700 c.c.
X-ray	50 r.					50 r.	

white blood cells 38,700. Differential; polymorphonuclears 25 per cent, lymphocytes 45 per cent, mononuclears 5 per cent, eosin 5 per cent, myelocytes 10 per cent, lymphoblasts 10 per cent. This was not considered abnormal for a newborn infant.

*Necropsy Report.**—Only the essential pathologic findings are reported. The histopathologic picture had been altered by the agonal invasion of *Clostridium welchii*. This terminal infection had caused areas of extensive necrosis with gas formation.

The body was that of a 29-year-old, fairly well-nourished, pale, white female. Cutaneous petechiae were distributed over the body. The lymph nodes of the anterior cervical triangles, the axillae, and inguinal regions were enlarged, discrete, and moderately firm.

Leucoblastic infiltrations were present in the form of discrete and confluent, pin-head-sized nodules throughout the myocardium, lungs, hyperplastic mammary glands, liver, kidneys, uterus, ovaries, uterine tubes, gastrointestinal tract, pancreas, and suprarenal glands. There was considerable pulmonary edema present. *Clostridium welchii* were isolated from the heart blood and spleen.

It is not within the scope of this paper to discuss the histogenesis of blood cells or the etiology of the leucemias. Although cognizant of the debatable question of identification of the type cell present in any given case of acute leukemia, we are inclined to believe this patient suffered from the lymphatic form of the disease. This assumption is based upon (1) daily study of the blood smears stained with Wright's stain, Giemsa's stain and Goodpasture's peroxidase reaction. (2) Absence of Auer's bodies. (3) The distribution of the leucoblastic cells as well as their cytoarchitecture. The marrow of the sternum, ribs and femur was firm and pale gray red.

Microscopic Description.—Bone marrow (femur): Few fat cells were present. There was marked hyperplasia of the undifferentiated cellular syncytium with beginning basophilia of the cytoplasm of the reticulum cells. The chromatin structure had become more condensed. There were many free transitional forms in the veins and sinuses characterized by mononuclear, nongranular basophilic cells. The two cell types which are present in the greatest numbers are:

1. A large cell with a narrow rim of basophilic protoplasm surrounding a large nucleus. The nucleus was either irregular, round, slightly indented, or kidney-bean in shape, and occupied a slightly eccentric position with the excavation directed toward the larger accumulation of protoplasm. The nuclear membrane was coarsely outlined. In the nuclei there were various sized chromatin particles scattered widely apart in a large quantity of clear nucleoplasm. One or several nuclei were seen. Single nucleoli were situated near the nuclear indentation.

2. A smaller and more basophilic mononuclear nongranular cell with a hyperchromatic, coarse, granular, or slightly leptochromatic nucleus with a distinct nuclear membrane containing nucleoli and surrounded by a slight pink-blue narrow rim of cytoplasm. Many of these cells were in mitoses. These two types of im-

*Autopsies were done on mother and babe by Dr. E. L. Benjamin, the pathologist of the Evanston Hospital.

mature lymphocytes were present in far greater numbers than were other cytologic elements. They were distending the small veins, the sinuses and extrasinusoidal reticulum. Rarely was a promyelocyte or myelocyte present. Relatively few erythrogonia and erythrocytes were present. An occasional histiocyte containing waste pigment and pyknotic nuclear material was seen. Pyknotic fragmented nuclear material was seen lying free in the reticulum fibers.

Irregular focal areas of degeneration and necrosis were present throughout the bone marrow. The centers of such areas contained many large bacilli with flat ends (*Cl. welchii*).

Lymph Nodes.—The cervical, axillary, inguinal, tracheobronchial, hepatic and to a lesser extent the periaortic and mesenteric lymph nodes were most noticeably involved. They ranged from 1.5 cm. to 2.5 cm. in diameter. The tracheobronchial lymph nodes were anthracotic. The others were pale gray. All were soft and enveloped by an intact capsule.

Microscopic Description.—All of the nodes examined displayed a diffuse reticulum cell hyperplasia with formation of immature lymphocytes. The primary and secondary follicles were indistinguishable. The trabeculae and capsule were heavily infiltrated with the type cell. The subcortical sinuses were filled with lymphocytes, histiocytes, and macrophages. The tremendous crowding of the leukemia infiltration rendered reticulum almost indistinguishable in some areas of the cortex and medulla. Mitoses of the lymphocytes were numerous. The small intrapulmonic lymph nodes still retained a trace of their normal architecture.

Spleen.—Weight 952 gm. The capsule was smooth. Surfaces made by sectioning, everted. The uniform red pultaceous substance was crepitant and somewhat spongy. The extensive degeneration by the agonal invasion of *Cl. welchii* rendered the sections unfit for microscopic study.

Reference to standard textbooks on obstetrics gave very little information as to prognosis and management. A desire for further knowledge prompted this review of the literature. It was found that the last review in this country was made in 1925 by Bower and Clark, who collected 17 cases. Kosmak, in 1921, had described 12. Since then more complete collections have been made in Europe by Neumann and Hofstein. The latest and most inclusive review was made in Italy by Garrassi in 1934 who found 59 cases. Not all of these were sufficiently clear for study. He gave credit to Debiassi for most of his collection and added several more. The authors have been able to find 74 cases, including those mentioned by the above authors, at least 8 of which have been published since Garrassi's study. To this series our own case is added, which brings the total to 75. Thirteen of this number had only bibliographic mention or were not reported in sufficient detail. Nine others were well enough described to include but were not classified. Thus we have 62 cases on which to base this study.

It was found that all cases were divided into two main groups, namely, acute and chronic. All of the chronic cases were myelogenous. Russell reported a case of chronic lymphatic leukemia, but because of the short duration of the disease and the early death of the patient we have included it in the acute group. Certainly it could be called subacute. There were 8 cases in the acute group which were called acute lymphogenous, including our own. Eleven were myelogenous. Two were diagnosed as acute hemocytoblastic and two others were not differentiated.

ONSET IN RELATION TO GESTATION

In the 25 acute cases it was believed the onset most often occurred during gestation. Only 5 started before pregnancy and but one of these as long as three months.

Eighteen cases started after conception, 7 in the first half and 10 in the last half of pregnancy. The month was not stated in one. The average time of onset was the fifth month. The time of onset was not mentioned in two others.

The onset in the 28 chronic cases was most often prior to conception. In 15 this varied from one to five years; in 3 from six months to a year and less than six months in one. In 3 cases it was not stated how long before. Five women had their first symptoms during pregnancy, 3 in the first half and one in the last half of gestation. In one the month was not stated. In one other no mention of the time of onset was made. When the onset was during pregnancy the average was in the fourth month.

TABLE II. ONSET OF LEUCEMIA IN RELATION TO GESTATION

	CHRONIC CASES	ACUTE CASES
Prior to Gestation		
1 yr. to 5 yr.	15	0
6 mo. to 1 yr.	3	0
Less than 6 mo.	1	4
Not stated	3	1
During Gestation		
First 4½ mo.	3	7
Last 4½ mo.	1	10
Not stated	1	1
Unknown	1	2

TABLE III. WHEN DELIVERED

PERIOD OF GESTATION	CHRONIC CASES	ACUTE CASES
Term	14	5
Premature 7 to 8½ mo.	6	10
Immature 4½ to 7 mo.	4	6
Abortion 4½ mo. or less	3	0
Undelivered—died	1	4

WHEN DELIVERED

In the acute cases four women died before delivery. Five went to term, 10 delivered prematurely (seven to eight and one-half months), 6 immaturely (four and one-half to seven months), and none aborted.

Of the chronic cases 1 woman died before delivery. Fourteen went to term, 6 delivered prematurely, 4 immaturely, and 3 aborted.

HOW DELIVERED

In the acute cases 15 delivered spontaneously. Six had operative deliveries, including 2 cesarean sections, 2 forceps deliveries and 1 version and extraction.

Among the chronic cases there were 22 spontaneous births, 3 induced abortions and 2 operative deliveries, including a cesarean at eight months and a hysterotomy at five months. Three of the spontaneous labors were induced.

HEMORRHAGE

In the acute cases hemorrhage was reported only five times. In but one case was it said to have been fatal. In another case bleeding occurred from the clitoris which was controlled with difficulty.

TABLE IV. HOW DELIVERED

	CHRONIC CASES	ACUTE CASES
Spontaneous term	22	15
Induced abortions	3	0
Operative	2	6
Undelivered	1	4

TABLE V. HEMORRHAGE

	NOT FATAL	FATAL
Chronic cases	7	0
Acute cases	4	1

In the chronic cases there was no fatality from hemorrhage during delivery. It was only reported seven times. Most authors commented on the lack of bleeding in delivery in both groups.

MATERNAL RESULTS

Only two women lived as long as five weeks after delivery in the acute cases, 14 died within fifteen days, 5 died in labor, and 4 died undelivered, a maternal mortality rate of 100 per cent.

The result for the mothers was strikingly different in the chronic cases. Twenty-three were alive two and one-half months after delivery, though 5 of these were dead within eight months. Four died in the puerperium and 1 died undelivered, a maternal mortality rate of 17.8 per cent.

In the 9 unclassified cases two women lived more than two and one-half months, 2 died within fifteen days of delivery, and another in five weeks. One was still alive and pregnant when the case was reported. The fate of 3 was not stated. Thus in the 58 patients delivered where the fate of the mother was stated, the mortality was 51.7 per cent, including deaths within two and one-half months after delivery.

FETAL RESULTS

No woman in the acute group had more than one pregnancy and there were no multiple births. Eight babies lived, 17 died, a fetal mortality rate of 68 per cent. Four of these died in utero and 13 were stillborn or were neonatal deaths. The principal cause of death was prematurity.

In the 28 chronic cases there were 33 pregnancies and 35 babies; 21 lived, 12 died or were stillborn, 5 viable and 7 not viable. One died in utero and in another the result was not stated. The fetal mortality rate was 37.1 per cent. The fate of the babies was remarkably good when delivered after the seventh month. None of the babies in either group had leucemia.

TABLE VI. MATERNAL RESULTS

	CHRONIC CASES	ACUTE CASES	UNCLASSIFIED CASES
Lived 2½ plus mo.	23	0	2
Died undelivered	1	4	0
Died in labor	0	5	0
Died within 15 days	4	14	2
Died within 5 weeks	0	2	1
Fate not given	0	0	3
Still alive and pregnant	0	0	1

TABLE VII. FETAL RESULTS

	CHRONIC CASES	ACUTE CASES	UNCLASSIFIED CASES
Pregnancies	33	25	9
Children	35	25	9
Lived	21	8	5
Died, 7 plus mo.	5	7	0
Died, under 7 mo.	7	6	2
Died, in utero when mother died undelivered	1	4	0
Fate not given	1	0	1
Mother still alive not delivered	0	0	1

TABLE VIII. ACUTE LEUCEMIAS

CASE	AUTHOR	YEAR	AGE	PARA	RELATION OF ONSET TO GEST.	PERIOD GESTATION DELIVERY		HEMORR.	RESULTS	
						WHEN	HOW		MOTHER	CHILD
1	Kerstein-Hilbert	1893	37	v	7th mo.	Term	Spont.	None	Died 3rd stage	Stillborn
2	Merttens	1900	30	i	4½ mo.	Undeliv.	-	-	Died with first pains	Stillborn
3	Lazarus and Fleischmann	1905	40	xii	4th mo.	5 mo.	Spont.	Fatal 3rd stage	Died 3rd stage	Stillborn
4	Bostetter	1906	23	i	7th mo.	Undeliv.	-	-	Died 7th month	Nonviable
5	Thaler	1914	40	ix	6th mo.	Term.	Spont.	None	Left hospital ill; probably died	Undelivered Stillborn
6	Petersen	1914	24	i	6th mo.	8 mo.	Spont.	None	Died few hr. P.P.	Lived
7	Lindbrones	1920	25	iii	2nd mo.	Undeliv.	-	-	Died undelivered	Lived?
8	Kosmak	1921	25	iii	3rd mo.	Undeliv.	-	-	Died undelivered	Stillborn
9	Kosmak	1921	35	iv	?	5 mo.	Ind. spont	None	Died 15th P.P. day	Lived?
10	Fleischmann	1923	30	iii	Prior	8 mo.	Cesarean	None	Died 11th P.P. day	Stillborn
11	Frank	1924	32	i	7th mo.	Term	High forc.	None	Died 6th P.P. day	Lived?
12	Allen	1928	20	i	3rd mo.	7 mo.	Vers. & ext.	Yes	Died 5th P.P. day	Stillborn
13	Saidd (2nd)	1931	25	?	1 mo. prior	8 mo.	Spont.	None	Died P.P. Atony	Died
14	Mann	1931	23	iv	2 mo. prior	8 mo.	Spont.	None	Died 5th P.P. day	Lived
15	Debiasi (2nd)	1931	15	i	7th mo.	8 mo.	Spont.	Yes	Died 11th P.P. day	Lived 56 d.
16	Held	1931	38	iv	?	Term	Extract.	None	Died 3rd stage	Stillborn
17	Heim	1932	26	?	3rd mo.	Term	Spont.	None	Died 8th P.P. day	Lived
18	Russell	1933	22	iii	3rd mo. prior	8½ mo.	Spont.	3rd stage	Died 5 wk. P.P.	Lived
19	Hüssy	1934	35	iii	During preg.	7½ mo.	Cesarean	None	Died 24 hr. P.P.	Lived
20	Traina	1937	28	i	3 mo. prior	5 mo.	Spont.	None	Died 2nd P.P. day	Stillborn
21	Zanella	1937	25	ii	4th mo.	6 mo.	Spont.	None	Died 3rd stage	Stillborn
22	Zanella	1937	22	i	5th mo.	6 mo.	Spont.	None	Died 8th P.P. day	Stillborn
23	Mehta	1937	18	i	7th mo.	7½ mo.	Low forc.	None	Died 2nd stage	Stillborn
24	Grier	1938	29	ii	4½ mo.	6½ mo.	Spont.	None	Died 27 hr. P.P.	Died in 12 d.
25	Wallgren	?	29	i	7th mo.	7½ mo.	Spont.	410 c.c.	Died 11th P.P. day	Stillborn

TABLE IX. CHRONIC LEUCEMIAS

CASE	AUTHOR	YEAR	AGE	PARA	RELATION OF ONSET TO GESTATION	PERIOD GESTATION DELIVERY		HEMORR.	RESULTS	
						WHEN	HOW		MOTHER	CHILD
1	Cameron	1888	36	vii	2 yr. prior	7 mo.	Spont.	None	Lived	Lived
2	Singer	1888	32	iii	Prior concep.	7 mo.	Ind. Spont.	None	Lived	Lived
3	Laubenberg	1891	32	vii	Prior concep.	5 mo.	Spont.	None	Died—40 hr.	Nonviable
4	Schroder	1898	26	viii	Prior concep.	6 mo.	Ind. Spont.	None	Lived	Nonviable
5	Joachim	1906	39	?	7 mo. prior	Term	Spont.	None	Lived	Lived
6	Savarre	1909	27	iii	3rd month	Term	Spont.	None	Lived	Lived
7	Savarre	1909	30	v	6th month	Term	Spont.	None	Died—11th d.	Stillborn
8	Kleinberger	1913	39	?	2½ yr. prior	Term	Spont.	None	Lived	Lived
9	Melnikoff and Tsonakion	1913	?	?	?	Term	Spont.	None	Lived	Lived
10	Gasser	1914	38	iii	7½ mo. prior	5 mo.	Ind. Spont.	10th d.	Lived 8 mo.	Nonviable
11	Renon and Degrais	1920	?	i	1 yr. prior	Term	Spont.	None	Lived	Lived
12	Meurer	1921	?	ix	1 yr. prior	8 mo.	Spont.	None	Lived	Twins—lived
13	Hausam	1922	28	ii	4 yr. prior	8½ mo.	Spont.	From clitoris	Lived 4 mo.	Lived
14	Chiari and Daut- witz	1924	27	i	1 yr. prior	Term	Spont.	None	Lived	Lived
15	Thamer	1925	28	ii	5 yr. prior	8 mo.	Cesarean	None	Died 11th d.	Stillborn
16	Bower and Clark	1925	24	i	5 yr. prior	Term	Spont.	None	Died—few hr.	Lived
17	Bower and Clark	1925	25	?	3rd month	-	No deliv.	None	Died 7th mo.	-
18	Neumann	1928	32	v	4 yr. prior	3 mo.	Ind. abort.	Yes	Lived 3¼ mo.	Nonviable
19	Ridder	1930	34	Mult.	3 yr. prior	Term	Spont.	None	Lived 2½ mo.	Lived
20	Neumann	1930	?	ii	2 mo. prior	3 mo.	Ind. abort.	Yes	Lived	Nonviable
21	Saidl	1931	35	iii	2 yr. prior	5 mo.	Hysterotomy	Yes	Lived	Nonviable
22	Webber	1931	38	iii	2 yr. prior	Term	Spont.	None	Lived 5 mo.	Twins—lived
23	Recek	1931	25	i	2 yr. prior	7 mo.	Spont.	10th d.	Lived	Died
24	Hofstein	1932	28	iv	2 yr. prior	2 mo.	Ind. abort.	None	Lived	Nonviable
25	Kaplan et al.	1932	26	ii	2½ yr. prior	Term	Spont.	None	Lived	Lived
26	Neumann	1932	35	iv	In 2nd mo.	Term	Spont.	None	Lived	Lived
27	Rydzewska	1932	37	Mult.	During preg.	Term	Spont.	Yes	Lived	Lived
28	Garrasi	1934	27	ii	7 mo. prior	Term	Spont.	None	Lived	Lived

TABLE X. INCOMPLETE DATA—NOT CLASSIFIED

CASE	AUTHOR	YEAR	AGE	PARA	RELATION OF ONSET TO GESTATION	PERIOD GESTATION DELIVERY		HEMORR.	RESULTS	
						WHEN	HOW		MOTHER	CHILD
1	Paterson	1870	?	i	5th month	Term	Spont.	Yes	Lived 10 days	Lived
2	Paterson	1870	?	i	5th month	Term	Spont.	Yes	Lived 14 days	Lived
3	Paterson	1870	?	iv	5th month	Term ?	Spont.	?	?	Lived
4	Ingle	1880	33	?	?	?	Spont.	?	?	Lived
5	Stillman	1890	34	vi	?	?	?	?	?	?
6	Sutcliffe	1914	21	i	?	Ectopic 3 weeks	Laparot.	Yes	Lived 1 mo.	-
7	Renon and Degrais	1920	?	?	?	5½ mo.	Spont.	?	?	Nonviable
8	Jimenez G. de la Serrana	1921	40	vii	3 yr. prior				Still pregnant when reported	-
9	Debiasi	1931	27	iii	?	Term	Spont.	None	Lived	Lived

Cases With Bibliographic Mention Only or Not Leucemic

1. Greene	1888	6. Ohlson	1925	10. Lammers	1929
2. Jaggard	1890	7. Kaplan	1927	11. Labhardt	1932
3. Herman	1900	8. Bruggeman	1928	12. Pontoni	1937
4. Schenk	1922	9. Geller	1928	13. Donati	1937
5. Nagy	1924				

The course of the disease in the acute cases was quite short, comparable with the duration frequently quoted when pregnancy was not a factor. When the disease started during gestation the average life expectancy was about ten weeks. And since the average month of onset was the fifth, death usually occurred before term could be reached, the average being 7.3 months.

The course of the disease in the chronic cases was about the same as that commonly stated when pregnancy was not involved. Most of the women had the disease for two years and nine months before conception. As the average time when delivered was 7.4 months, thus the average duration of the disease was three years, 4.4 months. As 18 women were still alive when their cases were reported they probably lived longer than four years with leucemia in spite of one or more pregnancies. Of the 4 women who died in the puerperium 2 had leucemia for nearly six years when delivered, which is certainly near the end of life expectancy for any chronic case. Thus we can say that the course is not terminated fatally by pregnancy unless in the late years of the chronic disease. There is usually, however, an exacerbation of symptoms with pregnancy and a remission after delivery.

TREATMENT OF LEUCEMIA

Many forms of therapy have been employed for the cure of leucemia, namely, arsenic, benzol, sulphur, iodine, x-ray, radium, thorium, ultraviolet rays, endocrines, splenectomy and grafting of the spleen. In acute cases nothing has been successful. Blood transfusions give a temporary increase in hemoglobin and red blood cells. In the chronic forms, arsenic, x-rays, and radium have been successful in producing temporary remissions in the early years of the disease. Blood transfusions are helpful as stated above and also decrease bleeding and coagulation times. After repeated x-ray treatment a resistance develops which voids beneficial effects. In the acute cases x-ray may be harmful. In our case the patient was made more uncomfortable even though a definite reduction in the lymphoblasts was accomplished.

SUMMARY OF CONDUCT

Any woman with leucemia should be advised against pregnancy. Some authors even advise sterilization. In this series of acute cases very few became pregnant with leucemia in progress, and in these the disease was not present for longer than three months prior to conception. The symptoms are so grave and the course so short that pregnancy is not likely after the disease has once begun.

In the chronic forms pregnancy should be avoided, because of the acute exacerbations which occur at the time. Occasionally death is sudden after delivery, especially when taking place in the later stages of the illness. Fortunately some of these women are sterile. Only one case of chronic lymphatic leucemia with pregnancy has been reported.

Some authors attribute this to the extensive infiltration of the ovaries and endometrium which interferes with ovulation and implantation of the ovum. This does not seem to be so in the chronic myelogenous type as five women have become pregnant more than once. Should a woman, knowing her condition, insist on becoming pregnant, she may be allowed to do so, provided that the disease has not been present too long and that she be observed closely. X-ray therapy may cause a remission and might produce good results.

Should a woman be pregnant when the disease is discovered, what course should be advised? In the chronic forms the pregnancy may be allowed to continue and x-ray therapy employed. If the disease is of

recent origin the immediate prognosis for mother and baby is good. If of several years' standing the prognosis is not as good but no interference should be attempted. Some authors disagree with this, as Hofstein, Saidl and Neumann, who advise interruption in early pregnancy. We agree with Garrassi who advises against it. A premature or nonviable baby is the result and the mother is not benefited.

In the acute forms no therapy produces even a remission of symptoms. Some authors state that x-ray therapy in these cases merely aggravates the condition. X-ray sickness adds to the patient's discomfort. Interruption of pregnancy only shortens the woman's life and results in premature babies. Blood transfusion aids the secondary anemia, obviates loss of blood and increases coagulation time. It is a palliative measure. If the disease is present in the last trimester, induction of labor or cesarean section is justifiable to save the baby when the mother is near death.

CONCLUSIONS

1. The frequency of chronic and acute forms in this series is nearly the same, being 28 for the former and 25 for the latter; 9 cases were unclassified.
2. The course of the chronic cases may be as long as six years, during which time some women have been pregnant more than once. Exacerbation is the rule during pregnancy.
3. The course of the acute cases was remarkably short and all women died during pregnancy, labor or the puerperium.
4. Only one case of chronic lymphatic leucemia has been reported. All the other chronic cases were of the myelogenous type.
5. The majority of acute cases were myelogenous, the ratio with those of the lymphatic type being 11 to 8.
6. Premature labor is frequent in the acute cases, less frequent in the chronic cases.
7. The prognosis for the babies is good in the chronic cases after viability, less favorable in the acute cases because of the frequency of premature delivery.
8. None of the babies showed evidences of leucemia.
9. Hemorrhage during delivery of the baby and the placenta was conspicuously uncommon. No women died of uterine hemorrhage in the chronic cases and only one in the acute cases.
10. No treatment of leucemia has been satisfactory. In the chronic forms x-ray apparently aids in producing a temporary remission of the leucocytosis and the symptoms. Blood transfusion has a very transient effect on secondary anemia but is the only treatment of value in the acute leucemias.
11. Pregnancy should be avoided when leucemia is known to be present. Only in the chronic forms may it be permitted if the woman insists and if her condition is explained to her.
12. Interference with pregnancy does not help the mother in either form. It only tends to produce premature or nonviable babies. In the acute forms it shortens the mother's life.

13. Premature induction of labor or cesarean section is justifiable when near term to save the baby and when the mother is near death.

14. Age and parity had no influence in these cases.

REFERENCES

- (1) *Paterson, R.*: Edinb. M. J. 15: 1073, 1869-70. (2) *Cameron, J. C.*: Am. J. M. Sc. 95: 28, 1888. (3) *Idem*: Am. J. M. Sc. 100: 479, 1890. (4) *Sänger, M.*: Arch. f. Gynäk., Berl. 33: 161, 1888-9. (5) *Greene, J. L.*: New York M. J. 47: 144, 1888. (6) *Jaggard, W. W.*: Med. News, Philadelphia 57: 49, 1890. (7) *Stillman*: Quoted by Jaggard, Med. News, Philadelphia, July 19, 1890. (8) *Laudenburg, C. E.*: Arch. f. Gynäk., Berl. 40: 419, 1891. (9) *Kirstein, E.*: Königsberg i. Pr., 1893. (10) *Hilbert*: Deutsche med. Wchnschr., 1893. (11) *Schröder, H.*: Arch. f. Gynäk., Berl. 57: 26, 1898. (12) *Merttens*: Monatsschr. f. Geburtsh. u. Gynäk. 12: 345, 1900. (13) *Herman, G. E.*: (Abstr.) Tr. Obst. Soc. Lond. (1901) 43: 234, 1902. (14) *Lazarus, P., and Fleischmann*: Deutsche med. Wchnschr., Leipz. u. Berl. 42: 1209, 1905. (15) *Bostetter*: Zentralbl. f. Gynäk., p. 265, 1906. (16) *Joachim, G.*: Ztschr. f. klin. Med., Berl. 60: 27, 1906. (17) *Luzzato, A. M., and Viana, O.*: Riv. Veneta di Scienze Med. 24: 2, 1907. (18) *Savare, M.*: Ginecologia, Firenze 6: 129, 1909. (19) *Keienberger, C.*: Strahlentherapie, Berl. u. Wien. 2: 573, 1912. (20) *Melnikoff, G. I., and Tsomakion, F. F.*: Russk. Vrach, S-Peterb. 12: 294 and 315, 1913. (21) *Thaler*: Zentralbl. f. Gynäk., No. 29, p. 1029, 1914. (22) *Peterson, A.*: Arch. f. Gynäk., Berl. 103: 272, 1914. (23) *Gasser, L.*: 8°. München, 1914. (24) *Sutcliffe, Lionel E.*: Brit. M. J. 2: 570, 1914. (25) *Tanton, J.*: Bull. et Mém. Soc. de chir. de Par. 43: 1437, 1917. (26) *Renon, L., and Degrais*: Bull. et mém. Soc. med. d. hop. de Par. 44: 1511, 1920. (27) *Lindbrones*: Acta med. Scandinav., 1920. Quoted by Wallgren: J. A. M. A. 76: 1439, 1921. (28) *Kosmak, G. W.*: AM. J. OBST. & GYNEC. 1: 485, 1920. (Discussion, p. 521.) (29) *Meurer, R. J. T.*: Nederl. Tijdschr. v. Geneesk. 2: 1440, 1921. (30) *Idem*: Nederl. Tijdschr. v. Verlosk. en Gynaec., Haarlem 28: 310, 1922. (31) *Jimenez G. de la Serrana, M., and Haro, F.*: Med. iberica, Madrid 15: 97, 1921. (32) *Wallgren, A.*: Acta med. Scandinav., Stockholm 54: 133, 1920. (33) *Hausam, E.*: München. med. Wchnschr. 69: 1627, 1922; Nov. Abst., J. A. M. A. 80: 364, 1923. (34) *Schenck*: Long Island M. J. 17: N. 4. (35) *Fleischmann, C.*: Zentralbl. f. Gynäk., p. 1277, 1923. (36) *Nagy, T.*: Gyogyaszat, No. 51, 1924. (37) *Frank, K. G.*: Zürich, 1924. (38) *Chiari, R., and Dautwitz, F.*: Wien. Arch. f. inn. Med. 11: 475, 1925; No. Abs.: J. A. M. A. 86: 317, 1926. (39) *Thamer, Hans*: Marburg, 1925. (40) *Bower, J. O., and Clark, J. H.*: AM. J. OBST. & GYNEC. 9: 207, 1925. (41) *Ohtsson, Inez*: Acta gynec. Scandinav., Helsingfors 3: 317, 1924. (42) *Joachim, G.*: Wien. Arch. f. inn. Med. 12: 603, 1926. (43) *Kaplan, A.*: J. akush. i zhensk. boliez 38: 785, 1927. (44) *Allan, W.*: AM. J. OBST. & GYNEC. 16: 112, 1928. (45) *Geller*: Gyn. Gesellschaft zu Dresden, Sitzung am 20. Nov., 1928. (46) *Brüggemann, F.*: Deutsche med. Wchnschr., Berlin & Leipzig, p. 1796-98. (47) *Neumann, H. O.*: Ztschr. f. Geburtsh. u. Gynäk. 94: 412, 1928. (48) *Idem*: Zentralbl. f. Gynäk. 54: 2443, 1930. (49) *Idem*: Deutsche med. Wchnschr. 58: 292, 1932. (50) *Ridder*: München. med. Wchnschr. 77: 2057, 1930. (51) *Lammers, H.*: Nederl. Tijdschr. v. Geneesk. 1: 316, 1929. (52) *Saidl, J.*: Časop. lékař. česk. 70: 949, 1931; also: Zentralbl. f. Gynäk. 55: 3053, 1931. (53) *Mann, B.*: AM. J. OBST. & GYNEC. 22: 416, 1931. (54) *Debiasi, E.*: Folia gynae. 28: 455, 1931. (55) *Weber, T.*: Rev. ostetr. (Rumena) 10: 112, 1931. (56) *Recek, V.*: Časop. lékař. česk. 70: 93, 1931. (57) *Held, E.*: Rev. franç. de gynéc. et d'obst. 26: 543, 1931. (58) *Hofstein, J.*: Strasbourg-med. 91: 611, 1931; also, Gynec. et obst. 25: 45, 1932. (59) *Kaplan, I. I., and Connery, J. E.*: Am. J. M. Sc. 183: 209, 1932. (60) *Heim, K.*: Zentralbl. f. Gynäk. 56: 22, 1932. (61) *Labhardt*: Oberrheinische Gesellschaft f. G. und G. Sitzung 26 marzo 1932 in Basel. (62) *Rydzewska, J.*: Ginek. polska 11: 707, 1932. (63) *Russell, H. K.*: AM. J. OBST. & GYNEC. 25: 493, 1933. (64) *Garrassi, G.*: Riv. ital. di ginec. 16: 295, 1934. (65) *Hüssy, P.*: Schweiz. med. Wchnschr. 64: 629, 1934. (66) *Pontoni, L.*: Minerva med. 1: 415, 1937. (67) *Traina Rao, G.*: Clin. ostet. 39: 76, 1937. (68) *Zaneta, S.*: Zentralbl. f. Gynäk. 61: 763, 1937. (69) *Donati, A.*: Folia clin. et biol. Brasil, anno I, No. 1, p. 47. (70) *Mehla, C.*: J. Obst. & Gynaec. Brit. Emp. 44: 328, 1937.

DISCUSSION

DR. HOWARD ALT.—I would like to praise part of the treatment and criticize another part. It appears that the transfusions did this patient a great deal of good, as on the third day her temperature began to come down, and on the fifth or sixth

day it was normal. The red cell count increased from two to four million. The white count after the last transfusion was 218,000, while the initial count was 410,000.

Just before discharge from the hospital she received an x-ray treatment. X-ray therapy is contraindicated in patients with acute leucemia, for if the dose is large, death may occur. On readmission to the hospital, the white count was low, but her condition was much worse. She again had a high fever and an increase in the purpura. A week or ten days later she received a second x-ray treatment, which was followed by the onset of labor within twenty-four hours. X-ray treatment has been used to induce labor, so it seems quite likely that the x-ray caused labor to begin in this case. It is possible that, if transfusions had been given once or twice a week and the x-ray omitted, the patient's life could have been prolonged sufficiently to obtain a viable infant. If acute leucemia occurs early in pregnancy, as Dr. Grier said, no interference should be attempted. If it occurs after the fifth month of pregnancy, it is frequently possible to obtain a live baby. In subacute leucemia the mother should be supported with blood transfusions until the fetus is viable.

I do not agree, however, with Dr. Grier on the management of pregnancy in chronic leucemia. It is reported that there is often an acceleration of the leucemia during pregnancy with improvement after the uterus is emptied. For this reason, it would seem best to terminate a pregnancy occurring early in chronic leucemia. The patient has enough of a load with the leucemia without adding the extra burden of pregnancy. If pregnancy occurs late in the course of chronic leucemia, the patient should of course be allowed to deliver spontaneously.

There are two main types of treatment in chronic myeloid leucemia: one is x-ray and the other arsenic. X-ray therapy should be withheld during pregnancy, as it cannot be given without danger to the fetus. Arsenic will produce a temporary remission in chronic myeloid leucemia, and at the same time will not hurt the fetus.

DR. HARRY A. RICHTER.—This patient's past history gives nothing of significance as an etiologic factor. There is a note of chronic otitis media and mastoiditis, following scarlet fever in childhood, but chronic infections have not been proved to be etiologic factors in leucemia.

Two years ago, three months after she had given birth to a normal boy, physical examination of this patient was negative and the blood picture normal. It would seem correct therefore that this case should be classed as "acute." The disease probably started during the course of the last pregnancy, or shortly before, the pregnancy causing an exacerbation of the disease.

The interruption of pregnancy during acute leucemia is attended by risk of hemorrhage and infection and often hastens the eventual fatality. It is generally considered that all forms of treatment in acute leucemia are of no avail, although blood transfusions tend to keep up the hemoglobin and red count and have less adverse effects than x-ray therapy, with its dramatic response in the reduction of white cells, glandular enlargements, and diminution in the size of the spleen and liver. Leucemic patients have little resistance to infection, and in acute leucemia, infection is usually present at the onset.

DR. C. D. HAUCH.—I wish to report a leucemia in a pregnant woman admitted to the Evangelical Hospital. She had had a severe leucemic crisis between her first and second pregnancies, but there were no definite symptoms of leucemia during the pregnancy. Therapeutic abortion was suggested but was advised against by the obstetric consultant. Pregnancy continued to term. Labor and the puerperium were normal. The baby is about one year old. The mother now has another leucemic crisis. No x-ray treatment was given or advised during pregnancy, but she has had two radiation treatments since.

DR. GRIER (closing).—The classification of leucemia is for the hematologist to decide, but from an obstetric viewpoint the division into acute and chronic is all that is necessary. Some of these so-called acute cases must have been really subacute.

The x-ray we used in this case may have done some harm. Her life expectancy at best was rather short with any therapy. The x-ray certainly did not aggravate her general condition and the leucocytosis was improved.

There have been only two men who have seen as many as three cases of leucemia with pregnancy, so I do not think any one man has had enough experience to take a decided stand. All of these conclusions I have drawn have been from the literature.

As to the interruption of pregnancy, I still believe it is not the thing to do. In cases where it was done the outcome for the patient was just as bad as when it was not done. In the early stages of the chronic group alone there may be some excuse for it. The cases allowed to go to term on the other hand did very well except where they had had the disease for five or six years.

GRANULOSA CELL TUMORS

WITH THE REPORT OF A 34 POUND SPECIMEN AND A REVIEW

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ALTHOUGH granulosa cell neoplasm of the ovary had been described as early as 1855⁸ the tumor did not receive the well-deserved attention it now commands until Robert Meyer's contribution in 1915. Since that time, however, Robinson, King, Novak, TeLinde, Schiller, Neumann and other investigators have made substantial additions to this gynecologic entity which, in view of the 300 cases reported, can no longer be considered as new. Consequently, in presenting our material, historic details will be summarily dismissed as these have been carefully considered in papers by Bland and Goldstein and others.

HISTOGENESIS

The concept of Robert Meyer, that these tumors arose from granulosa cell rests in the ovarian hilus is no longer tenable in its original form. Recent experiments by Butterworth have shown that granulosa cell tumors can be produced in mature female mice by the use of roentgen rays. The tumors, histologically and functionally entirely analogous to the granulosa cell tumors of women, appeared to spring directly from degenerating follicular epithelium.

CLINICAL FEATURES

Sixty per cent of granulosa cell tumors occur after the menopause, 30 per cent occur between puberty and the climacterium, and 5 to 10 per cent occur before adolescence. In childhood these tumors give rise to precocious menstruation with early sexual and somatic development. During the period of sexual maturity they produce either amenorrhea per se or amenorrhea followed by profuse and continuous menses. After the menopause, granulosa cell neoplasm gives rise to a periodic pseudomenstrual type of bleeding in 90 per cent of the cases.

The basis for these symptoms is to be found in the tremendous quantities of estrin elaborated by these tumors in all age groups. The hor-

mone can be demonstrated in the blood and urine of patients who have granulosa cell neoplasm and in almost unbelievable amounts in extracts of tumor tissue. Its action on the uterus is the production of myo-hyperplasia with a thick, boggy, proliferative type of endometrium often containing cysts. The exact mode by which a different syndrome is produced in the different age groups is not well understood.

PATHOLOGY

Ninety per cent of granulosa cell tumors are unilateral, 90 per cent are solid, and 90 per cent are of a relatively very low grade of malignancy. They vary in size from the pin head nodules described by TeLinde to large masses weighing 34 pounds (15.4 kg.) as in Case 1 described below. They appear to be well encapsulated. The cut surface has the homogeneous, granular appearance of liver sausage and this appearance allows one to make a correct gross diagnosis in 50 per cent of the cases. Microscopically the cylindroid, folliculoid and diffuse types of cellular pattern are so well known as to merit little description. They do not represent separate entities but may be found mixed even in the same microscopic slide.

MATERIAL

In a study of the solid and solid-cystic group of ovarian tumors removed surgically at The Mayo Clinic from 1905 to 1937, 30 examples of granulosa cell neoplasm were encountered. The specimens were all formalinized—a fact which precluded their study from the standpoint of hormone content. The clinical and pathologic data, however, are sufficiently clear to make possible an analytic study. The tumors were studied in gross, and interesting specimens were photographed. Multiple sections were then cut and stained routinely with hematoxylin and eosin. Lipoid stains were employed whenever indicated. Where possible, sections were made of the endometrium and of the unaffected ovary.

CASE 1.—A single, white nullipara, aged 37 years, was admitted to the clinic April 28, 1916, complaining of an abdominal tumor and amenorrhea. Her family and personal histories were negative. Menses had begun at the age of fourteen years and had been normal for ten years. For the succeeding twelve years she had had amenorrhea, except for an occasional episode of bleeding, moderate to profuse in amount. Eight years prior to admission she had first noticed a pelvic tumor which had steadily increased in size. Weakness, palpitation, and dyspnea had been present for six months.

Positive physical findings were the presence of marked emaciation and a huge pelviabdominal tumor. Positive laboratory data were a hemoglobin reading of 40 per cent and mild albuminuria.

At operation, May 5, 1916, a huge, solid, left ovarian tumor was removed. Adhesions or metastasis was not noted.

The postoperative course was uneventful and the patient returned home on the twelfth day. At a subsequent examination, in 1921, her menses were recorded as being normal. Neither at this time nor at a later visit, in 1935, was there any evidence of recurrence following this local operative procedure.

Grossly, the tumor weighed 34 pounds (15.5 kg.). It was firm, encapsulated, somewhat lobulated and grayish brown. On section, large, cystic regions of degeneration and hemorrhage were found. However, examination of the solid portions revealed granular homogeneity so characteristic that a diagnosis of granulosa cell neoplasm was made before the microscopic confirmation.

Microscopically, sections from various parts of the neoplasm all presented the same architectural pattern; namely the so-called cylindroid type of neoplasm, according to Meyer's classification (Figs. 1, 2, and 3).

CASE 2.—A married, white primipara, aged 31 years, presented herself for examination Feb. 8, 1921. Her family and personal histories had been entirely negative. Menses had begun at the age of fifteen years and had been normal until two and a half years prior to her registration, when flow had become scanty in amount and periods spaced further apart. Two years before the patient's admission, her menses had ceased entirely. For eight months a dull pain had been present in the left lower abdominal quadrant. For six months the patient had noticed bilateral mammary tenderness.

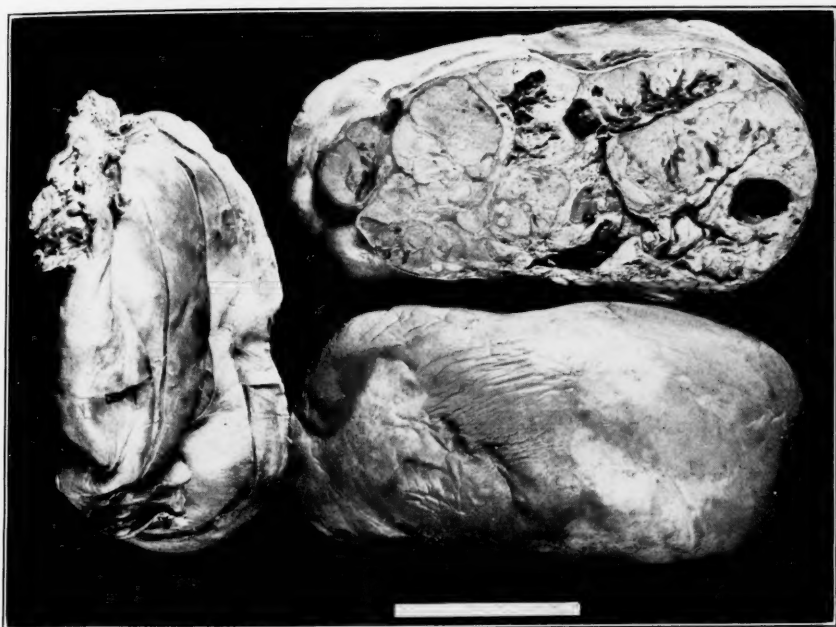


Fig. 1.—(Case 1.) Surface and sectional views of a granulosa cell tumor weighing 34 pounds (15.5 kg.).

Positive physical findings were limited to the presence of a left ovarian tumor and moderate mammary enlargement, with tenderness. Laboratory data were negative.

At operation, Feb. 21, 1921, a solid, left ovarian tumor was found. A frozen section was made rapidly and the unusual character of the neoplasm recognized. Local resection therefore was elected and the patient was given a postoperative course of mild roentgen therapy.

Subsequent correspondence revealed that regular menses became established within four months. The patient went through a normal pregnancy five years later. She is now alive, without recurrence, sixteen years after operation.

Grossly, the specimen consisted of the left tube attached to a solid, encapsulated tumor 5 cm. in diameter. The surface was smooth and grayish brown. On section the mass was solid throughout and of a homogeneously granular texture.

Microscopically, in the capsule were several corpora albicantes and other ovarian remnants. The tumor was composed of small, round, granulosa-like cells with

large basophilic nuclei. The predominant architectural unit was "cylindroid" with transitions to the "folliculoid" and "diffuse" types of Robert Meyer. The tube gave evidence of chronic inflammatory thickening.

CASE 3.—A white multipara, aged 50 years, registered at the clinic June 30, 1931. Her family and personal histories had been negative. Menses had been regular until her climacterium at the age of forty years. One year prior to her registration menses apparently recurred; the bleeding, which occurred monthly, was profuse. Weakness and loss of 10 pounds (4.5 kg.) in weight, completed her list of complaints.

Positive physical findings were an enlarged uterus and a right ovarian tumor. Laboratory data were negative.

At operation, July 3, 1931, hysterectomy was performed, with removal of both adnexa for a right ovarian tumor. The postoperative course was smooth and, follow-

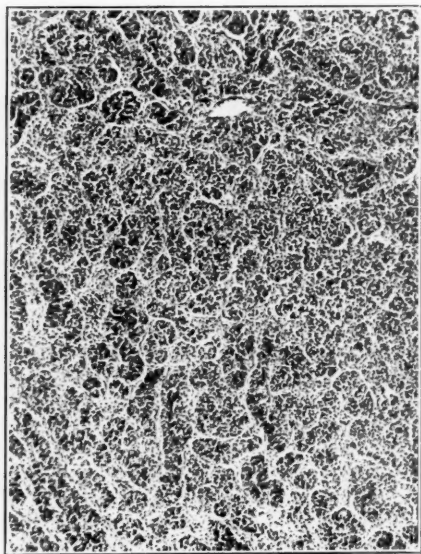


Fig. 2.

Fig. 2.—(Case 1.) The general "cylindroid" unit of cellular arrangement. ($\times 80$.)

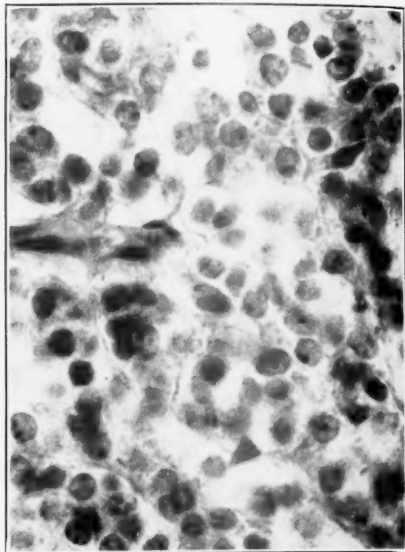


Fig. 3.

Fig. 3.—(Case 1.) The granulosa-like character of the tumor cells. ($\times 720$.)

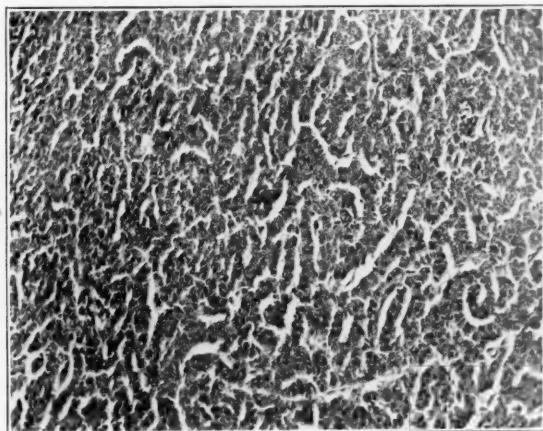


Fig. 4.—(Case 3.) The "moire-silk" pattern of tumor architecture. ($\times 125$.)

ing a short period of roentgen therapy, the patient returned home. In follow-up studies this case is classified as a "five-year cure."

The uterus was markedly hypertrophied, measuring 9 by 7 by 5 cm. It contained multiple small fibroids and the endometrium was polypoid. Both tubes were chron-

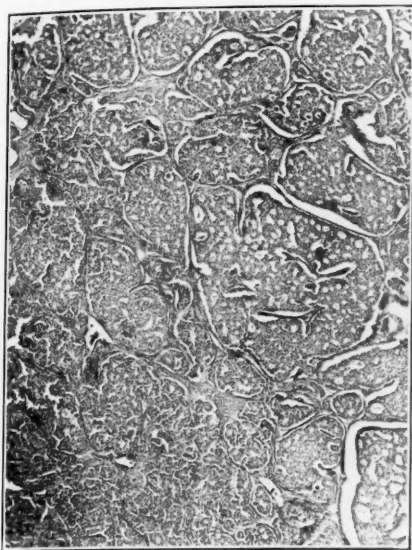


Fig. 5.

Fig. 5.—(Case 8.) An almost pure "folliculoid" type of cell pattern. ($\times 40$.)

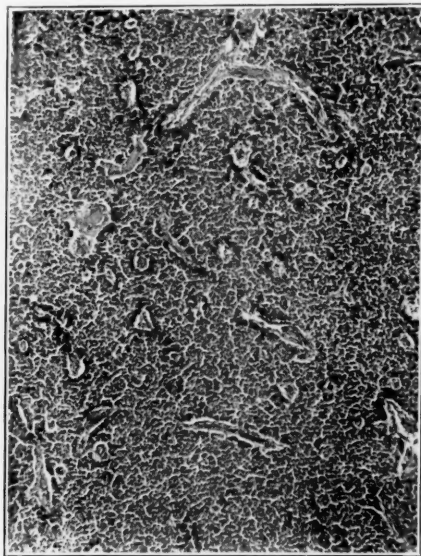


Fig. 6.

Fig. 6.—(Case 9.) A mixed "folliculoid" and "cylindroid" type of cell pattern. ($\times 120$.)



Fig. 7.

Fig. 7.—(Case 9.) Several "follicles" containing "ovum-like" bodies. ($\times 310$.)



Fig. 8.

Fig. 8.—(Case 17.) Three different types of cell architecture in the same field. ($\times 125$.)

ically inflamed. The left ovary was fibrocystic and atrophic. The right ovary was replaced by a tumor, 19 cm. in diameter, and of a gross character similar to that described for the previous cases. Regions of cystic degeneration were present on section.

Microscopically the "cylindroid" pattern predominated, illustrating the so-called moire-silk modification. The endometrium was proliferative in type, contained cysts and reflected the action of estrin (Fig. 4).

CASE 4.—A white nullipara, 37 years of age registered Oct. 15, 1912. Family and personal histories were negative. Menses had begun at the age of fifteen years and had been regular for ten years. Following this, for a period of twelve years, menses had been irregular and there had been a tendency toward hypomenorrhea. During the year prior to registration the patient had menstruated only three times.

Examination revealed a large, movable tumor in the cul-de-sac. At operation, Oct. 17, 1912, a local procedure was carried out for removal of a left ovarian tumor.

After operation normal menstrual regularity became established and was maintained for sixteen years. At a recent examination, twenty-three years after the original operation, this patient was in good health.

Grossly, the tumor was a solid, encapsulated neoplasm measuring 10 by 10 by 9 cm. Here again the appearance of the tumor suggested the correct diagnosis.

Microscopically the picture was that of a granulosa cell neoplasm of the mixed folliculoid and cylindroid patterns.

CASES 5 TO 30.—These are summarized in Table I (Figs. 5 to 8).

TABLE I. DATA ON PATIENTS WITH GRANULOSA CELL TUMOR* (PATIENTS MORE THAN 50 YEARS OF AGE)

CASE	AGE	NUMBER OF PREGNANCIES	SYMPTOMS	DURATION SYMPTOMS	PATHOLOGIC FINDINGS		
					FI-BROIDS	CYSTIC ENDO-METRI-UM	OUTCOME
1	63	2	Periodic bleeding	10 years	+	+	Living, 6 years
2	72	4	Bleeding	2 weeks	0	+	Died, 5½ years later†
3	60	0	Periodic bleeding	3 months	+	+	Living, 6 years
4	60	4	Periodic bleeding	3 months	0	+	Living, 8½ years
5	70	0	Periodic bleeding	4 years	0†	—	Living, 4½ years
6	58	3	Continuous bleeding	6 months	+	+	Living, 10 years
7	61	1	Irregular spotting	20 years	+	+	Living, 3½ years
8	51	0	Periodic bleeding	1½ years	+	+	Living, 9 years
9	55	0	Periodic bleeding	4 years	+§	+	Died, 10 months later
10	62	1	Periodic spotting	5 years	0	+	Died, 10 days later
11	59	0	Irregular bleeding	5 years	0†	—	Living, 7 years
12	58	3	Irregular and periodic bleeding	4 years	0	+	Living, 17 years
13	56	4	Menorrhagia and metrorrhagia	1 year	0	+	Not traced
14	69	3	Slight irregular bleeding	3 years	0	+	Living, 15 years
15	77	2	Bronchial pneumonia	1 week	0	+	Necropsy
16	61	10	Bleeding	1 month	0	+	Living, 10 years
17	62	5	Recurrent periodic bleeding	8 months	+	+	Living, 11 years

*With the exception of Case 15 in which operation was not performed, all patients were subjected to total abdominal hysterectomy and bilateral salpingo-oophorectomy.

†Carcinoma of fundus uteri.

‡Died of unknown cause.

§Died of cerebral hemorrhage.

COMMENT ON CASES

The average age of these patients was 51 years; the extremes were 17 and 77 years. Eighteen patients, or 60 per cent, were in the postmenopausal age, four were in what might be termed the "menopausal" age of 40 to 50 years, while 30 per cent were in the period of fertility. Marriage and pregnancy did not appear to bear any constant relation to the incidence of tumor development. Of the 28 married patients, 22 had been pregnant one time or more. On the other hand, that the tumors produced temporary sterility was evidenced by the fact that in no case did pregnancy ensue in the interval between the onset of symptoms and the time of operation. That this period of sterility was temporary is illustrated by Case 2, wherein a local operative procedure was followed by normal pregnancy.

Abnormal menstrual manifestations were present in 27 of the 30 cases. In the postmenopausal age, bleeding was the presenting symptom in 16 of the 18 cases. This symptom alone had been periodic in 12 cases, for periods varying from two weeks to twelve years. In several instances

TABLE II. DATA ON PATIENTS WITH GRANULOSA CELL TUMOR (PATIENTS 40 TO 50 YEARS OF AGE)

AGE	NUMBER OF PREGNANCIES	SYMPTOMS	DURATION SYMPTOMS	OPERATIVE PROCEDURE	PATHOLOGIC FINDINGS		OUTCOME
					FIBROIDS	CYSTIC ENDO-METRIUM	
48	2	Menorrhagia	5 years	Local†	-	-	Not traced
50	2	Menorrhagia	1 year	2 local operations	-	-	Reurrence?
40	0	Amenorrhea	1 year +	Total*	0	+	Living, 8 years
47	3	Amenorrhea and menorrhagia	2 years	Total	+	+	Living, 5 years

*Total abdominal hysterectomy and bilateral salpingo-oophorectomy.

†Operative resection of tumor only.

TABLE III. DATA ON PATIENTS WITH GRANULOSA CELL TUMOR (PATIENTS LESS THAN 40 YEARS OF AGE)

AGE	NUMBER OF PREGNANCIES	SYMPTOMS	DURATION SYMPTOMS	OPERATIVE PROCEDURE	PATHOLOGIC FINDINGS		OUTCOME
					FIBROIDS	CYSTIC ENDO-METRIUM	
33	1	Amenorrhea	2 years	Local†	-	-	Died, 3 days p.o.
38	5	Menorrhagia	1 year	Total*	0	+	Living, 9 years
		Amenorrhea and menorrhagia	5 years				
25	1	Amenorrhea	18 mo.	Total	+	+	Living, 9 years
		Metrorrhagia	3 mo.				
17	0	Amenorrhea	1 year	Local	-	-	Living, 2 years
26	1	Constant flow	1 year	Local	-	-	Living, 20 years

*Total abdominal hysterectomy and bilateral salpingo-oophorectomy.

†Operative resection of tumor only.

the patients described these episodes as being accompanied by the manifestations of "normal" menstruation such as uterine cramps, tenderness of the breasts, and low backache.

In the menopausal age amenorrhea of long or of short duration usually was followed by recurrence of vaginal bleeding, again periodic. In one of the cases amenorrhea and menorrhagia occurred alternately over a period of two years.

In the group of cases in which the patients were less than forty years of age, amenorrhea was a symptom of unusual frequency; it occurred in seven instances. In Case 1, amenorrhea (except for occasional spotting) had been present for twelve years and antedated by four years the appearance of palpable pelvic tumor. Amenorrhea followed by bleeding was a feature in two cases. Menorrhagia and metrorrhagia were present in one instance. Of the patients in this group who underwent local resection of the tumor, all except one experienced a return of normal menses following operation.

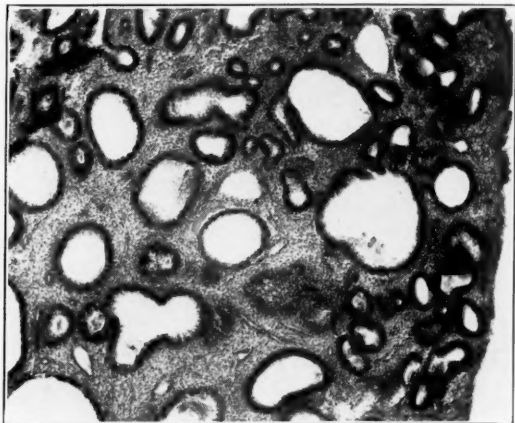


Fig. 9.—(Case 24.) The "Swiss cheese" type of endometrium found in connection with granulosa cell tumors. ($\times 125$.)

Little need be said of the physical findings in these cases. An enlarged uterus was recognized in the majority of instances and a palpable adnexal tumor in most of the cases. Clinical anemia was present in those cases in which the patients suffered from menorrhagia and metrorrhagia. Evidence of hyperthyroidism was observed in two instances; this raises a question of a possible etiologic relationship between hyperthyroidism and the ovarian tumor.

The neoplasms were unilateral in every case although in one instance, there was a small dermoid cyst involving the contralateral ovary. Ascites was noted in one of the cases but metastasis was not observed in any. Adhesions usually were absent but on two occasions were found to be extensive and associated with tumors which had become twisted on their pedicles.

Among older patients hysterectomy, with bilateral salpingo-oophorectomy, was the usual procedure, while among younger patients a

more conservative type of operation was elected. In eight instances local resection of the tumor was carried out. Postoperative irradiation was given in approximately 60 per cent of the cases.

Seventeen uteri were available for study. Hypertrophy was a definite feature in 14 cases. Leiomyomas, usually multiple, were present in 8 cases. Endometrial carcinoma was present in two cases and this again raises the question of its possible relation, etiologically, to ovarian neoplasm. In all of the remaining 15 of the 17 cases there was present a condition of polypoid-cystic change, with a definite Swiss-cheese pattern in 9 (Fig. 9).

The contralateral ovary was available for study in 17 instances. Absence of mature or maturing corpora lutea represented the only constant finding. A mild degree of follicular hyperplasia was present in two instances. One ovary was the seat of a small dermoid cyst but no example of a second granulosa cell tumor could be found.

Changes in the Fallopian tubes were not remarkable.

The incidence of malignancy in this series of cases is perhaps lower than the average for reported cases of granulosa cell tumors. One of the patients who is living has a definite, inoperable recurrent growth. Two of the patients we have been unable to trace. Two patients who had large tumors died from postoperative complications but metastasis could not be demonstrated. The remaining 25 patients are living and well, without recurrence, at periods of from two to thirty years after operation. Case 1 is illustrative of a granulosa cell tumor of a known duration of eight years. The tumor attained a weight of 34 pounds (15.5 kg.) without metastasizing. This patient is now alive twenty-two years after local resection of her tumor, followed by a course of mild roentgen therapy.

SUMMARY, CONCLUSIONS AND A SUGGESTION

1. The clinical and pathologic features of 30 granulosa cell neoplasms are presented.
2. These tumors are thought to arise from granulosa cell rests in the hilus of the ovary, or from degenerating Graafian follicles.
3. The tumor cell unit anatomically and functionally resembles the granulosa cell.
4. Folliculoid, cylindroid, and diffuse tumor cell patterns represent varying degrees of differentiation rather than separate entities.
5. A pathologic report of proliferative endometrium with cysts in a case of periodic, postmenopausal bleeding, should demand exploratory laparotomy even in the absence of a palpable pelvic tumor.
6. Granulosa cell tumors appear to be of a low grade of malignancy. The suggestion is made therefore that surgical procedures employed in the treatment of these tumors be conservative when the patients are young.

REFERENCES

- (1) *Acconci*: Quoted by Bland, T. B., and Goldstein, L. (2) *Bland, T. B., and Goldstein, L.*: Surg. Gynec. Obst. 61: 250, 1935. (3) *Blau, A.*: Arch. f. Gynäk. 128: 506, 1926. (4) *Butterworth, J. S.*: Am. J. Cancer 31: 85, 1937. (5) *Comp-*

ton, Beverley C.: AM. J. OBST. & GYNEC. 34: 85, 1937. (6) Daily, E. F.: Ibid. 26: 733, 1933. (7) Frank, R. T.: Am. J. Dis. Child. 43: 942, 1932. (8) Habbe, K.: Zentralbl. f. Gynäk. 55: 1088, 1931. (9) Iwanow, I. J.: Ztschr. f. Geburtsh. u. Gynäk. 115: 262, 1937. (10) von Kahlen, C.: Zentralbl. f. allg. Path. u. path. Anat. 6: 257, 1895. (11) King, E. S. J.: Surg. Gynec. Obst. 49: 433, 1929. (12) Klasten, E.: Zentralbl. f. Gynäk. 58: 204, 1934. (13) Meyer, Robert: AM. J. OBST. & GYNEC. 22: 697, 1931. (14) Novak, Emil: Ibid. 26: 505, 1933. (15) Robinson, M. R.: Ibid. 5: 581, 1923. (16) Rokitansky: Quoted by Bland, T. B., and Goldstein, L. (17) Schiller, W.: J. Obst. & Gynaec. Brit. Emp. 43: 1135, 1936. (18) Schiller, W.: Personal communication to the authors. (19) Schroeder, H.: Zentralbl. f. Gynäk. 46: 195, 1922. (20) Schroeder, Hans: Arch. f. Gynäk. 64: 193, 1901. (21) TeLinde, R. W.: AM. J. OBST. & GYNEC. 20: 552, 1930. (22) von Werdt: Quoted by Bland, T. B., and Goldstein, L.

A FIFTEEN-YEAR STUDY OF CESAREAN SECTION IN THE WOMAN'S HOSPITAL IN THE STATE OF NEW YORK*

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IN THE fifteen-year period from Jan. 1, 1923, to Jan. 1, 1938, 20,127 women, in the viable period of pregnancy, have been delivered in the Woman's Hospital in the State of New York. In this group are all deliveries at or beyond the twenty-eighth week of gestation. There were 9,712 of these women who were on the Ward Obstetrical service and 10,415 were private patients. There were 94 maternal deaths or an uncorrected maternal mortality of 0.45 per cent, with an uncorrected fetal mortality of 4.3 per cent. This includes stillbirths and neonatal deaths from all causes while the baby remained in the hospital. Prematurity or major deformities incompatible with life were the causative factors in nearly 60 per cent of these stillbirths and neonatal deaths.

The following is a review of the cesarean sections performed in these 20,127 delivered women. In the fifteen-year period covered by this study the obstetric ward service has been under the direction of ten attending and junior attending surgeons with their adjuncts and assistants. Approximately two-thirds of the private obstetric patients in the series have been delivered by this group of obstetricians, while the remaining one-third of the private obstetric patients have been delivered by a selected courtesy group of some 25 obstetric and gynecologic specialists.

Approximately 4,000 women in the 20,127 had some operative delivery other than prophylactic or low forceps, an operative incidence of 1:5 deliveries. This high incidence of operative interference is perhaps due to the fact that our facilities are limited and on the ward service preference is given to the admission of primiparas or to multiparas who have abnormalities or previous obstetric difficulties. On the private service are numerous consultants to whom are referred many patients who are considered abnormal by the general practitioner. In other words the material for study contains a higher incidence of abnormalities and obstetric complications than is encountered in general obstetric practice.

Approximately 800 in each 1,000 deliveries terminated spontaneously or by the use of prophylactic low forceps. In other words, 200 in each 1,000 women or 4,000

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in the total group of 20,127 delivered women, required assistance. In the slightly more than 16,000 spontaneous or prophylactic low forceps deliveries there were 32 deaths, a maternal mortality rate of 0.2 per cent, while in the 4,000 who had indicated operative deliveries there were 62 maternal deaths, a maternal mortality rate of 1.5 per cent. Spontaneous delivery, or prophylactic low forceps delivery in the hands of obstetric specialists, is the safest for both mother and baby. In this series the use of prophylactic low forceps was followed by better results to both mother and baby.¹ Mid- and high forceps deliveries (the high forceps operation being used very rarely) gave the next lowest maternal mortality, the maternal mortality being 17 deaths in 2,000 or approximately 0.81 per cent with total fetal mortality of 6 per cent, in these vaginal deliveries. Breech extraction or version and breech extraction had the highest maternal and fetal mortality rates. In 980 such deliveries the maternal death rate was 1.69 per cent while the fetal death rate was 20 per cent.

Some years ago in our follow-up of the delivered patients on the ward service we felt that our results in the more difficult vaginal deliveries were not entirely satisfactory. In the prolonged labors and difficult vaginal operative deliveries, we found a rather high incidence of birth injuries, stillbirths, and neonatal deaths. In addition the incidence of pelvic floor injury, cystocele, rectocele, and uterine prolapsus was not encouraging. We felt that many of these women would be faced with subsequent partial invalidism and later plastic operations with an additional risk to health and life. At this time the low flap cesarean section was being popularized. The advantages of this operation appealed to us and we began using it more frequently in the borderline cases usually after a trial labor. The results were so satisfactory that the method has been adopted as the operation of choice in all cesarean sections on the ward service and our indications for its use have been widened to include many of the so-called relative indications for cesarean section.

Cesarean section has not been in competition with spontaneous delivery or with delivery by prophylactic or low forceps. It has been in competition with the more difficult forceps operations and with breech extraction and version and breech extraction especially when labor was unduly slow or in the presence of moderate degrees of pelvic deformity or other obstetric and general complications.

Comparative incidence rates of cesarean section are shown in Table I.

TABLE I. COMPARATIVE INCIDENCE AND MORTALITY TABLES ON CESAREAN SECTION

			INCIDENCE	MORTALITY RATE
Fraser	1938	Montreal	1:44	3.0
Greenhill*	1930	Chicago	1:48	—
Skeel-Jordan	1932	Cleveland	1:44	7.15
Monhaupt	1932	Germany	1:45	—
Johnson and Smith	1931	Houston	1:36	14.4
Palmer	1934	Akron	1:41	4.5
Maxwell	1934	U. of Calif. Hosp.	1:21	3.0
Margeson	1929	Boston City Hosp.	1:29	3.4
Hawkes	1929	N. Y. Nurs. & Child's	1:62	3.6
Irving	1935	Boston Lying-in	1:35	3.1
	1938	Woman's Hospital	1:22	2.96

*Quoted by Fraser.

Our incidence of cesarean section is higher but our mortality rate is somewhat lower than average. I believe the general mortality rate of cesarean section is considered to be about 6 to 10 per cent. Certainly it will run considerably higher in the less well-equipped hospitals and in the hands of unskilled or occasional operators.

The number and incidence rate of cesarean section at the Woman's Hospital is shown in Table II. The incidence rate of cesarean section is consistently higher in the private patient group, general average on ward patients 1:29, private 1:18. The incidence rate of the past five or six years in the private group is unusually

TABLE II. NUMBER AND INCIDENCE OF CESAREAN SECTIONS, WARD AND PRIVATE CASES, BY YEARS, 1923-1937

	TOTAL DELIVERIES			CESAREAN SECTIONS			INCIDENCE OF CESAREAN SECTIONS		
	TOTAL	WARD	PRIVATE	TOTAL	WARD	PRIVATE	TOTAL	WARD	PRIVATE
1923	1,089	548	541	23	1	22	1:47	1:548	1:25
1924	1,197	537	660	23	8	15	1:52	1:67	1:44
1925	1,280	513	767	38	9	29	1:34	1:57	1:26
1926	1,329	527	802	32	11	21	1:42	1:48	1:38
1927	1,367	534	833	31	6	25	1:44	1:89	1:33
1928	1,315	536	779	27	7	20	1:49	1:77	1:39
1929	1,411	550	861	49	15	34	1:29	1:37	1:25
1930	1,377	586	791	46	24	22	1:30	1:24	1:36
1931	1,334	624	710	64	24	40	1:21	1:26	1:18
1932	1,422	741	681	80	35	45	1:18	1:21	1:15
1933	1,317	758	559	85	43	42	1:15	1:18	1:13
1934	1,330	771	559	88	34	54	1:15	1:23	1:10
1935	1,433	853	580	107	44	63	1:13	1:19	1: 9
1936	1,405	809	596	120	46	74	1:12	1:18	1: 8
1937	1,521	825	696	99	31	68	1:15	1:27	1:10
15 years	20,127	9,712	10,415	912	338	574	1:22	1:29	1:18

high. Perhaps good results with cesarean section has blinded us to the possibility of success by vaginal delivery in a certain number of this group.

Absolute indications for cesarean section are few. Pelvic deformity or contraction of such degree that the delivery of a child is impossible even after crushing or craniotomy, would be such an indication as would fixed tumors blocking the pelvis to an equal degree. All other indications must be considered as relative, since it would be possible to deliver the fetus, either dead or alive, through the birth canal, though at a terrific sacrifice in fetal life and the risk of excessive damage and permanent invalidism to the mother.

TABLE III. CHIEF INDICATIONS FOR CESAREAN SECTION

	TOTAL	WARD	PRIVATE
Abnormal pelvis	401	165	236
Previous cesarean section	191	77	114
Disproportion	146	50	96
Large baby	71	17	54
Toxemia	102	54	48
Eclampsia	5	1	4
Previous stillbirth and difficult delivery	190	74	116
Elderly primiparas	87	27	60
Cervical dystocia	235	85	150
Inertia uteri	32	8	24
Previous myomectomies	30	7	23
Breech presentation	43	18	25
Abnormal presentation	36	14	22
Tuberculosis	38	16	22
Tumor blocking pelvis	15	6	9
Placenta previa	75	33	42
Premature separation of placenta	22	7	15
Previous plastic repair	34	5	29
Myomas	36	10	26
Cardiac disease	60	34	26
Thyrototoxicosis	5	3	2
Psychoses	6	-	6
Attempted vaginal delivery	8	2	6
Bandl's ring	5	4	1
Maternal exhaustion	17	9	8
Prolonged sterility	15	2	13
Desire for sterilization	6	6	-

In the woman with a moderate pelvic deformity or disproportion or with complicating mild cardiac or other disease it may be entirely safe to allow a carefully supervised trial labor. If reasonable progress is made without undue maternal exhaustion or evidence of cardiac failure, this trial may go on to the real test of labor as defined by Williams¹³—this test being two hours of full dilatation with ruptured membranes and good uterine contractions. This to my mind is a purely mechanical test of whether the head will go through the pelvis and if the maternal organism will stand the strain of the process. Undue prolongation of labor with inefficient uterine contractions and slow dilatation of the cervix or premature rupture of the membranes markedly increases the risks to both mother and baby whatever the type of eventual delivery.

The chief indications for which cesarean section was done in this series are shown in Table III. It will be seen that many patients had more than one indication. The totals on the chart indicate the number of patients presenting a given indication.

Table IV gives a brief résumé of the obstetric history of our cesarean section patients to which is added the uncorrected fetal mortality table for all cesarean deliveries. The mortality rate of 2.62 compares favorably with the general mortality rate of 2.96. The majority of these patients had elective cesarean section without trial labor. Those patients having the third cesarean section had more than double the average mortality rate. The series is small and no conclusions are drawn.

TABLE IV. OBSTETRIC HISTORY OF PATIENTS

	NO. OF CASES	MATERNAL DEATHS		INFANT DEATHS		STILL- BIRTHS		TOTAL FETAL MORTALITY	
		NO.	RATE	NO.	RATE	NO.	RATE	NO.	RATE
Total	912	27	2.96	31	3.40	30	3.29	61	6.69
Primiparas	517	15	2.90	14	2.71	16	3.09	30	5.80
Multiparas	395	12	3.04	17	4.30	14	3.54	31	7.84
With previous cesarean sections*	191	5	2.62	5	2.62	5	2.62	10	5.24
1 previous cesarean	163	3	1.84	5	3.07	4	2.45	9	5.52
2 previous cesarean sections	26	2	7.69	-	-	1	3.85	1	3.85
3 previous cesarean sections	2	-	-	-	-	-	-	-	-
With previous vaginal delivery	204	7	3.43	12	5.88	9	4.41	21	10.29

*With or without previous vaginal deliveries also.

Table V gives the age of patients having cesarean section. The most favorable age group seemed to be in the second decade. In the small group of patients over 40 years of age, the maternal mortality rate, as well as the fetal mortality rate, was more than doubled. This study would indicate that the risk to both mother and baby is markedly increased in patients of 40 years or over.

TABLE V. AGE OF PATIENTS

	ALL CASES			PRIMIPARAS			MULTIPARAS		
	NO. OF CASES	MATERNAL DEATHS		NO. OF CASES	MATERNAL DEATHS		NO. OF CASES	MATERNAL DEATHS	
		NO.	RATE		NO.	RATE		NO.	RATE
All ages	912	27	2.96	517	15	2.90	395	12	3.04
Under 20 years	9	-	-	8	-	-	1	-	-
20-29 years	380	6	1.58	245	4	1.63	135	2	1.48
30-39 years	434	17	3.92	206	8	3.88	228	9	3.95
40 years and over	39	3	7.69	27	2	7.41	12	1	-
Not specified	50	1	2.00	31	1	3.23	19	-	8.33

Table VI shows the maternal and infant mortality rate according to the period of gestation.

TABLE VI. PERIOD OF GESTATION

	ALL CASES	28-38 WEEKS	38-40 WEEKS	OVER 40 WEEKS
No. of cases	912	168	693	51
Maternal deaths	27	2	20	5
Rate	2.96	1.19	2.89	9.80
Infant deaths	31	21	9	1
Rate	3.40	12.50	1.30	1.96
Stillbirths	30	11	15	4
Rate	3.29	6.55	2.16	7.84
Total fetal mortality	61	32	24	5
Rate	6.69	19.05	3.46	9.80

Between twenty-eight and thirty-eight weeks of gestation the maternal death rate was low but the fetal mortality was 3 or 4 times the general average. In gestation beyond forty weeks, there was a high maternal death rate, nearly 4 times the average for the total group and the fetal death rate was about twice the general average.

Table VII summarizes the maternal deaths with reference to the time of rupture of the membranes.

TABLE VII. CONDITION OF MEMBRANES

	NO. OF CASES	MATERNAL DEATHS	
		NO.	RATE
All cases	912	27	2.96
Membranes intact	622	15	2.41
Membranes ruptured	290	12	4.14
Less than 12 hours	116	5	4.31
12-24 hours	54	-	-
24 hours and over	73	7	9.59
Time not recorded	47	-	-
Premature rupture	37	3	8.11

In the large group of women with intact membranes at the time of cesarean section, the maternal death rate was below the average while the maternal death rate in those in whom the membranes were ruptured at the time of operation, the general maternal mortality was nearly double. When membranes had been ruptured for over twenty-four hours at the time of cesarean section, the maternal mortality rate was tripled. An interesting finding is the absence of any maternal deaths in a group of 54 women with ruptured membranes of between twelve and twenty-four hours. This may be due to the fact that these are uncomplicated cases in which a carefully supervised trial labor was attempted.

Table VIII reviews the maternal death rate in relation to the dilatation of the cervix.

TABLE VIII. CONDITION OF CERVIX

	NO. OF CASES	MATERNAL DEATHS	
		NO.	RATE
All cases	912	27	2.96
Undilated	543	12	2.21
Dilated	365	14	3.84
Less than 5 cm.	215	8	3.72
5-9 cm.	107	5	4.67
9 cm. and over (fully)	32	1	3.13
Amount not recorded	11	-	-
No cervix	4	1	25.00

It would seem that cervical dilatation had only moderate effect in increasing the death rate, although as full dilatation was approached, the maternal death rate was considerably above the average for the total group.

Table IX summarizes both the maternal and fetal mortality in relation to the duration of labor before the cesarean section was done.

TABLE IX. DURATION OF LABOR

	NO. OF CASES	MATERNAL DEATHS		INFANT DEATHS		STILLBIRTHS		TOTAL FETAL MORTALITY	
		NO.	RATE	NO.	RATE	NO.	RATE	NO.	RATE
All cases	912	27	2.96	31	3.40	30	3.29	61	6.69
No labor	457	11	2.41	25	5.47	13	2.84	38	8.31
After period of labor	455	16	3.52	6	1.32	17	3.74	23	5.05
Less than 6 hours	56	4	7.14	3	5.36	2	3.57	5	8.93
6-24 hours (incl.)	242	4	1.65	2	0.83	10	4.13	12	4.96
Over 24 hours	140	8	5.71	-	-	5	3.57	5	3.57
Time not recorded	17	-	-	1	5.88	-	-	1	5.88

In general the death rate is higher in those women having cesarean section after a period of labor as compared to the group who were cesareanized prior to the onset of labor. The fact that many of our more serious ante-partum complications such as placenta previa, toxemia, tuberculosis, and the more severe grades of cardiac disease were sectioned before labor, brings the death rate in total group of elective section to about the average figure. If these severe ante-partum complications are left out, the elective section group shows a very low death rate of approximately 1 per cent. In this series it would be possible to pick up several groups of 75 to 100 or more consecutive elective cesarean sections done in otherwise healthy women, without any maternal deaths. The low maternal mortality in the group of women having cesarean section after from six to twenty-four hours of labor, is again perhaps best explained on the grounds that these were otherwise healthy women in whom a carefully supervised trial labor was allowed. In the group of women who had twenty-four hours or more of labor, there was a rapid rise in maternal mortality.

Table X is a summary of the type of anesthesia used for cesarean section.

TABLE X. TYPE OF ANESTHESIA USED

	NO. OF CASES	MATERNAL DEATHS	
		NO.	RATE
Total	912	27	2.96
Inhalants	833	23	2.76
Gas, oxygen, ether	784	23	2.93
Ether	26	-	-
Gas, oxygen	19	-	-
Ethylene	1	-	-
Ether, chloroform	1	-	-
Chloroform	1	-	-
Chloroform and gas, oxygen, ether	1	-	-
Spinal	72	4	5.56
Alone	56	3	5.36
With inhalants	16	1	6.25
Local	3	-	-
Alone	1	-	-
With inhalants	2	-	-
Avertin	4	-	-
Alone	2	-	-
With inhalants	2	-	-

Practically all cesarean sections were done under inhalation anesthesia, usually gas, oxygen, and ether combination. Spinal anesthesia had the highest maternal mortality rate, though none were directly due to the anesthesia itself. Spinal anesthesia was used more frequently in the severely toxic cases or in mothers with known pulmonary

disease. The pulmonary complications in women having spinal anesthesia were comparable to those receiving inhalation anesthesia.

Table XI indicates the marked preference of the low flap cesarean especially in the ward service.

TABLE XI. WARD AND PRIVATE CASES BY TYPE OF CESAREAN SECTION

	TOTAL CASES	WARD		PRIVATE	
		NO.	PER CENT	NO.	PER CENT
Total cesarean sections	912	338	37.1	574	62.9
Low flap	620	253	40.8	367	59.2
Transverse incision	534	220	41.2	314	58.8
Vertical incision	75	28	37.3	47	62.7
Incision not specified	11	5	45.5	6	54.5
Classical	235	51	21.7	184	78.3
Latzko	34	23	67.6	11	32.4
Porro	17	9	52.9	8	47.1
Peritoneal exclusion	6	2	33.3	4	66.7

The transverse incision is highly favored for this operation. It is our belief that the bleeding is less with this incision and the danger of bladder or upper uterine segment involvement from extension of the incision avoided. In our series there has been only one bladder injury with this operation and this was in a patient on whom a vertical incision was made.

In the Latzko operation, accidental bladder injury occurred four times. In three of these the bladder was opened and in one the musculature only was damaged sufficiently to require repair. All of these patients healed well without complication referable to the bladder injury. In one of the Latzko operations, done after a prolonged labor, in a woman who had fever and a high Bandl's ring, there was an accidental injury to the ureter, apparently from disturbance with the blood supply, since she developed a ureterocervical fistula on the seventh day. This required subsequent operation about ten months later following which there has been no further urinary leakage. The uterovesical fold of peritoneum was accidentally opened 6 times in the Latzko operations. And, in 4 other patients this fold was deliberately incised and closed before opening the uterus, as recommended by Aldridge.¹³ In no case did this opening result in peritonitis.

In the Porro operations there was one ureteral injury which was repaired by transplant of the ureter into the bladder with complete recovery and good kidney function.

In the total group of 912 cesarean sections there were 165 incidental operations exclusive of the hysterectomies which, of course, were a part of the Porro operations. Forty of these patients had myomectomies, 114 had sterilization either by partial excision of the tubes or ligation of tubes. In recent years ligation by the Pomeroy method has been favored. One patient had an ovarian cyst removed at time of the section, and six had unilateral salpingo-oophorectomy. Only one patient had an associated appendectomy.

It has been a general policy to do as little operating as possible in association with cesarean sections. Bilateral ligation of the tubes seemed to add little to the morbidity or mortality. Since only 3 patients in the 165 who had additional operation with cesarean section died, our mortality rate was not increased.

One patient died after cesarean section plus myomectomy.

One patient died after cesarean section plus sterilization.

One patient died after cesarean section plus sterilization and myomectomy.

Table XII shows the mortality and morbidity associated with various types of cesarean section.

Low flap cesarean section had less than half the mortality of the classical section. Latzko section had a mortality equal only to the average mortality of the whole series. The Porro naturally had higher than average mortality rate due to the complications which indicate this type of operation. The peritoneal exclusion operation was done in a very small series and to my mind the maternal mortality rate shown here is not a fair indication of the worth of this operation in the presence of indications for its use.

TABLE XII. MORTALITY AND MORBIDITY BY TYPE OF CESAREAN SECTION

	NO. OF CASES	MATERNAL DEATHS		MATERNAL MORBIDITY	
		NO.	RATE	NO.	RATE
All types	912	27	2.96	277	30.37
Low flap	620	13	2.10	168	27.10
Classical	235	10	4.26	80	34.04
Latzko	34	1	2.94	19	55.88
Porro	17	1	5.88	8	47.06
Peritoneal exclusion	6	2	33.33	2	33.33

TABLE XIII. CHIEF CAUSES OF POST-PARTUM MORBIDITY

	CASES
Post-partum morbidity, all causes	277*
Sapremia	55
Unexplained temperature rise	38
Toxemia	4
Eclampsia	3
Septicemia	7
Metastatic abscesses	4
Parotitis	6
Pelvic sepsis, localized	18
Urinary infections	43
Urinary fistula	4
Peritonitis, general	6
Paralytic ileus	7
Hemorrhage and sec. anemia	34
Shock, post partum	4
Mastitis	26
Faulty wound union	43
Evisceration	1
Vascular disturbances	38
Heart conditions	9
Respiratory complications	31
Other complicating diseases	8

*One hundred twenty-one of these cases had ante-partum morbidity also.

Table XIII tabulates the major causes of post-partum morbidity associated with cesarean section. The accepted criteria for morbidity in this series has been a temperature of 100.4° F. on any two successive days after the first forty-eight hours postoperative. Also included in morbidity tables are faulty wound healing, urinary complications and various constitutional diseases. It will be noted that in the total group of 277 postcesarean morbid patients, 121 also had ante-partum morbidity.

Table XIV gives a summary of patients dying after cesarean section, showing the period of gestation, the incidence of previous cesarean sections, and also the type of examination made prior to a cesarean section.

TABLE XIV. SUMMARY OF DEATH CASES

	LOW FLAP	CLASSICAL	PERITONEAL EXCLUSION	PORRO	LATZKO
<i>Vaginal and Rectal Examinations</i>					
No examination	2	8	-	-	-
Rectal examination only	1	-	-	-	-
Vaginal examination only	5	2	1	1	-
Rectal and vaginal exam.	5	-	1	-	1
<i>Period of Gestation</i>					
30-36 weeks	1	1	-	-	-
38-40 weeks	7	9	2	1	1
Over 40 weeks	5	-	-	-	-
<i>Previous Cesarean Sections</i>					
	1	4	-	-	-

It will be noted that in 8 patients on whom no vaginal or rectal examination was made, there was death following classical cesarean section, while only 2 patients on whom no vaginal or rectal examinations were made, died subsequent to a low flap cesarean section.

This table also shows the rise in death rate in the post-mature patient. Five patients died who had had previous cesarean section, a mortality rate slightly over 2½ per cent or a little less than the general mortality rate for the whole series. It would seem that repeated cesarean section is no more dangerous than the primary cesarean section.

Table XV shows a tabulation of patients dying following cesarean section, classified as to the condition of the membranes and the duration of labor.

TABLE XV. SUMMARY OF DEATH CASES

	LOW FLAP 620	CLASSICAL 235	PERITONEAL EXCLUSION 6	PORRO 17	LATZKO 34
<i>Condition of Membranes</i>					
Membranes intact	4	9	2	-	-
Rupt. less than 12 hours	4	-	-	1	-
12-24 hours	-	-	-	-	-
24 hours and over	5	1	-	-	1
<i>Duration of Labor</i>					
No labor	2	9	-	-	-
Less than 12 hours	2	1	1	1	-
12-24 hours	1	-	-	-	-
24 hours and over	8	-	1	-	1

This table shows the superiority of low flap over classical cesarean section even with intact membranes. Again it shows the increased number of deaths after twenty-four hours of ruptured membranes. The best results are in the twelve- to twenty-four-hour group. This represents the group who were allowed a reasonable trial labor and in whom none of the major ante-partum complications were present. Also the increase in deaths after twenty-four hours of labor even though low flap section is chosen.

Table XVI gives a summary of the ante-partum complications and the causes of death in the 27 fatalities following 912 cesarean sections.

TABLE XVI. SUMMARY OF CAUSES OF DEATH

	LOW FLAP (620)	CLASSICAL (235)	PERITONEAL EXCLUSION (6)	PORRO (17)	LATZKO (34)
Peritonitis	3	1	-	1	-
Septicemia	1	3	2	-	-
Pulmonary embolism	3	-	-	-	-
Cerebral embolism	-	1	-	-	-
Mesenteric thrombosis	-	1	-	-	-
Coronary thrombosis	-	-	-	-	1
Myocardial failure	3	-	-	-	-
Hemorrhage and shock	1	3	-	-	-
Pneumonia	1	1	-	-	-
Collapse of lung	1	-	-	-	-
<i>Ante-partum Complications</i>					
Placenta previa	2	-	-	-	-
Toxemia	3	3	1	1	-
Cardiac disease	2	1	1	-	-
Sec. anemia	1	-	-	-	-
Tuberculosis	1	-	-	-	-
Acute yellow atrophy	1	-	-	-	-

Thirteen deaths followed the low flap operation done on 620 patients, 10 deaths followed the classical operation done on 235 patients. In the 13 deaths following the low flap operation, 5 are from causes directly traceable to the operation, the remaining 8 are from complications not directly connected with the type of delivery. While in the 10 deaths following the classical cesarean, 8 are from causes directly traceable to the operation while only two are from complications not directly associated with the type of delivery. The low flap group shows that 10 of the 13 mothers who died had major ante-partum complications which were factors in the fatal outcome while in the classical group only 4 of the 10 mothers who died had associated severe ante-partum complications. The classical operation in itself would seem to be more dangerous than the low flap operation.

Table XVII shows the maternal mortality rate in the group of 20,127 women tabulated by years for both ward and private patients; in addition, the cesarean deaths are likewise tabulated.

TABLE XVII. MATERNAL MORTALITY FOR CESAREAN SECTIONS AND ALL DELIVERIES WARD AND PRIVATE CASES, BY YEARS, 1923-1937

	MATERNAL DEATHS						CESAREAN SECTION DEATHS					
	TOTAL		WARD		PRIVATE		TOTAL		WARD		PRIVATE	
	NO.	RATE	NO.	RATE	NO.	RATE	NO.	RATE	NO.	RATE	NO.	RATE
1923	6	0.55	2	0.36	4	0.74	2	8.70	-	-	2	9.09
1924	2	0.17	2	0.37	-	-	-	-	-	-	-	-
1925	5	0.39	3	0.58	2	0.26	3	7.89	1	11.11	2	6.90
1926	7	0.53	3	0.57	4	0.50	2	6.25	1	9.09	1	4.76
1927	9	0.66	4	0.75	5	0.60	2	6.45	-	-	2	8.00
1928	10	0.76	4	0.75	6	0.77	2	7.41	1	14.29	1	5.00
1929	13	0.92	5	0.91	8	0.93	3	6.12	1	6.67	2	5.88
1930	8	0.58	5	0.85	3	0.38	1	2.17	1	4.17	-	-
1931	6	0.45	4	0.64	2	0.28	1	1.56	1	4.17	-	-
1932	7	0.49	3	0.40	4	0.59	3	3.75	1	2.86	2	4.44
1933	5	0.38	3	0.40	2	0.36	-	-	-	-	-	-
1934	3	0.22	2	0.26	1	0.18	2	2.27	2	5.88	-	-
1935	5	0.35	3	0.35	2	0.34	3	2.80	2	4.55	1	1.35
1936	6	0.43	3	0.37	3	0.50	2	1.67	1	2.17	1	1.59
1937	2	0.13	-	-	2	0.29	1	1.01	-	-	1	1.47
15 years	94	0.47	46	0.47	48	0.46	27	2.96	12	3.55	15	2.61

Deaths following cesarean section totaled slightly more than one-quarter of all deaths in the series. However, in two years 1924 and 1933 with two deaths and 5 deaths, respectively, none were due to cesarean section. While in 1927, 1928, 1929, 1930, with a total of 40 deaths, cesarean section was responsible for only 8 deaths; 1929 with the highest maternal mortality of the fifteen years and showing an incidence of cesarean section of 1:29 deliveries, yet only 3 of the 13 deaths followed cesarean section. In 1933 with a cesarean incidence of 1:15 deliveries there were no cesarean deaths although there were 5 maternal deaths following vaginal delivery. In general as the incidence of cesarean section increased there has been no corresponding increase in the maternal death rate. This can be proved by a comparison with the incidence in Table I. In fact the tendency has been to a lower general maternal mortality as the incidence of cesarean increased. This, I believe, is due to the performance of cesarean sections earlier in labor with the avoidance of prolonged labor and maternal exhaustion, in the presence of ruptured membranes or other complicating factors.

Fewer women are being allowed to become exhausted before delivery is made. Another important factor is the more frequent use of blood transfusion and other supportive measures. Blood donors are readily available and in a majority of cases a suitable donor is present in the hospital at the time of the cesarean section. If the hemoglobin and red blood cell counts are low a preoperative transfusion is given. Also patients are now treated for shock and restored to a reasonably fair condition before cesarean section is done. This is noticeably true in the treatment of placenta

previa and the severe degrees of premature separation of placenta with an improved maternal mortality whatever the type of delivery.

The total maternal mortality rate in 1937 is most gratifying. There were no deaths of ward patients in 825 deliveries with 31 cesarean sections.

A comment on the 27 deaths from all causes occurring in 912 cesarean sections may be ventured in no spirit of criticism but in an honest effort to evaluate the results in this long study. Some of the cases are my own. In the 10 deaths following classical cesarean section in 235 operations, there are 6 on which no comment is indicated, if one chooses to employ the classical operation for the elective cesarean section. In 4 of these cases I wish to make certain observations.

1. A patient in the private group on whom classical section was elected after eleven days of ruptured membranes, died of septicemia and peritonitis on the sixth day postoperative, with positive staphylococcus blood culture. This patient might have been safer with an earlier operation or possibly an extraperitoneal operation.

2. A patient in the private group who was treated for three and one-half weeks in the hospital with a blood pressure ranging from 190/100 to 210/130 and albuminuria from 1 to 6 gm. per liter. There was no improvement during this time. A classical section was done at thirty weeks because of a desire for sterilization. There was considerable bleeding and shock though no blood transfusion was given until shortly before death, twenty-four hours postoperative. Possibly an earlier induction of labor when the patient failed to respond to the toxemia treatment might have given a more favorable result.

3. A patient in the private group who had profuse bleeding at the time of the classical section, had uterine tamponade at time of operation. No transfusion until four hours later and the bleeding not controlled. In this case an earlier transfusion followed by repacking or possible hysterectomy might have been considered a better choice of procedure.

4. A private patient on whom an elective classical section was done. This patient had no blood count before operation and none until the fifth day postoperative when a marked anemia of 45 per cent with 2,500,000 red blood cell count was found. Then a 500 c.c. blood transfusion was given. No further blood count recorded and no further transfusion. This patient died on the tenth day of sepsis and abscess of parotid gland. Possibly earlier and more vigorous attention to the anemia might have prevented the lowered resistance and septic condition.

In the 13 deaths following 620 low flap cesarean operations, there are 4 on which no comment is indicated. Comments are made on 9 as follows:

1. A 39-year-old primipara, in the private group, with a myocardial weakness from fatty degeneration, who had sixty hours labor with cervical dystocia and disproportion. This woman died of cardiac and respiratory failure on the operating table. An earlier cesarean section before the exhaustion of labor would seem to be indicated.

2. A ward patient 33 years of age, multipara of 48 weeks' gestation with transverse position. Admitted and examined in the early stages of labor because of moderate vaginal bleeding. Examination by an intern stirred up an uncontrollable vaginal hemorrhage. An obstetrician was called who packed the vagina after a blood loss of approximately 2,500 c.c. Gum glucose was given immediately and a low flap section was done. Eleven-pound baby in good condition. Patient received a blood transfusion during the operation. Patient died one hour later of hemorrhage and shock. Better results might have been expected if this patient had been suspected of a possible placenta previa when she went to forty-eight weeks' gestation with a transverse presentation. Our rule now is no examination of bleeding patients until a donor is ready and then examination only by a member of the attending staff with everything in readiness for operation if indicated. No patient is subjected to cesarean section until she has reacted from her shock through the use of blood transfusions and such other methods as are indicated.

3. Ward patient, para v, forty-two weeks' gestation, thirty-eight-hour trial labor with marked disproportion. Two previous stillbirths. This patient died of peritonitis on her third day. This trial labor was too long for safety even with low flap operation. In view of the history of stillbirths, etc., an elective cesarean section might better have been chosen.

4. Private patient at forty-one weeks' gestation. A medical induction of labor following extensive myomectomies. Sixty-four hours trial labor and temperature of 101° F. followed by low flap cesarean section. Peritonitis and death on fifth day postoperative. The advisability of an induction and prolonged trial labor in a woman with extensive myomectomy wounds, is questionable. No transperitoneal operation is safe after sixty-four hours of labor and in the presence of fever.

5. A ward patient with myocardial disease and a placenta previa. Died six hours postoperative of hemorrhage and shock. Transfusion was not given until more than four hours postoperative. This again demonstrates the advisability of having a donor in attendance at time of operation in all placenta previa cases.

6. A ward patient. This patient had had a previous cesarean section. Her pregnancy was unsupervised. She first presented herself after twenty-four hours of labor plus ruptured membranes. She died on the eleventh day postoperative of peritonitis. She had marked secondary anemia when admitted and received one blood transfusion before operation and three after operation. This death may be charged to the neglect of the patient herself since she delayed placing herself under medical care.

7. A private patient. Treated during pregnancy for mitral stenosis and an elective section was planned. The patient delayed entering the hospital until she had been in labor for ten hours when she had beginning decompensation. She died one hour postcesarean. Again, this may be charged to the patient's negligence, since she had been warned of the dangers and plans had been made for elective section before or at the onset of labor.

8. A ward patient, forty-eight hours in labor with ruptured membranes. Cervical dystocia with head above brim in R.O.P. position. Died on the third day postoperative of peritonitis. The selection of an extraperitoneal section might have been a better choice.

9. A private patient, 35 years old, primipara, at thirty-eight weeks' gestation. Toxemia of pregnancy with early yellow atrophy of liver. Elective low flap section. Patient had central placenta previa not previously suspected. Died six hours postoperative of shock and a moderate retroplacental hemorrhage of 300 c.c., behind the flaps of the operation. Transfusion was of no avail. Autopsy showed fairly advanced yellow atrophy of liver. With the known tendency to oozing and bleeding in cases of yellow atrophy of the liver it might be well to give a preoperative blood transfusion even though there was no anemia.

The greatest problem of obstetrics is in the management of the borderline indications for cesarean section. With intact membranes and an otherwise relatively normal woman, a trial or even real test of labor is comparatively safe. With ruptured membranes, slow cervical dilatation or rigid cervix and maladaptation of the head, the finest of obstetric judgment is needed. There is great danger in delaying the operation in these borderline cases until the mother is exhausted and an easy prey to infection and complications, and the baby likely to succumb, whatever the type of delivery.

To conclude this laborious study and presentation, I can find no fairer expression of my own views on the use and abuse of cesarean section than those of Mellor¹⁴: "Unquestionably too many cesareans are performed where the method of delivery should have been otherwise especially when the operation is done under adverse conditions and by relatively untrained obstetric surgeons. Poor results in obstetrics are caused most often by the abuse rather than the proper use of obstetric surgery. Watchful waiting is an essential virtue in obstetric management, but look out for eriminal procrastination just around the corner."

Since this study includes both private and ward patients, I hereby acknowledge, with thanks, the courtesy of the many obstetricians involved, and of the Chief Surgeon of the hospital, for permission to use this material.

REFERENCES

- (1) Aldridge, Albert H.: *AM. J. OBST. & GYNEC.* 30: 554, 1935. (2) Fraser, John R.: *Surg. Gynec. Obst.* 66: No. 2A, 1938. (3) Greenhill, J. P.: *AM. J.*

OBST. & GYNEC. 19: 613, 1930. (4) *Skeel, A. J., and Jordan, F. F.*: Ibid, 23: 172, 1932. (5) *Monhaupt, Gerhard*: Zentralbl. f. Gynäk. 56: 2416, 1932. (6) *Johnson, R. A., and Smith, Fred B.*: South. M. J. 24: 724, 1931. (7) *Palmer, George A.*: AM. J. OBST. & GYNEC. 28: 557, 1934. (8) *Mosher, George C.*: Surg. Gynec. Obst. 45: 655, 1927. (9) *Maxwell, Alice F.*: West. J. Surg. 42: 14, 1934. (10) *Margerson, Reginald D.*: New England J. Med. 200: 1141, 1929. (11) *Hawkes, E. M.*: AM. J. OBST. & GYNEC. 18: 393, 1929. (12) *Irving, Fred C.*: J. Connecticut M. Soc. 1: 483, 1937. (13) *Aldridge, Albert H.*: AM. J. OBST. & GYNEC. 33: 788, 1937. (14) *Mellor, Lester R.*: State J. New York, p. 1763, 1938.

DISCUSSION

DR. ALBERT H. ALDRIDGE.—Success in the handling of obstetric patients should not be judged entirely by the mortality rate which accompanies a method of delivery. It should also include an estimation of results in patients that survive.

In recent years, good results with low flap cesarean section have encouraged members of the Woman's Hospital staff to adopt this method of delivery for an increasing number of patients who have cardiac disease, the toxemias of pregnancy, tuberculosis, placenta previa and cervical dystocia. Cesarean section has also been chosen for the delivery of certain cases in which the outlook for babies delivered by vagina was definitely problematical. These cases included those with breech presentation in primiparas, especially when the babies were unusually large or the pelvis borderline in size; those showing fetal distress during the first stage of labor, and those with evident fetomaternal disproportion and especially those with histories of previous complicated deliveries or unsuccessful pregnancies. The results of suprapubic delivery in all these types of cases as compared to delivery by the vaginal route has convinced us that cesarean section is occasionally justifiable in the interest of the baby as well as of the mother, if cases are carefully selected.

In some of these cases the benefits and safety of cesarean section depend upon application of the method either as an elective procedure or early in labor. This undoubtedly has resulted in the delivery of some cases in the series by cesarean section which might have been safely delivered by vagina.

Material for this study was collected over a period of years during which much experience has been acquired to guide obstetricians in the selection of patients to be delivered by cesarean section; methods for the routine preparation of patients for operation have improved and the technique of cesarean section has been perfected. Unsatisfactory results in the series serve to emphasize the importance of careful selection of patients to be delivered by cesarean section and the necessity of meticulous preparation of patients for operation.

DR. BENJAMIN P. WATSON.—I was especially interested in comparing the results at the Woman's Hospital with our experience at Sloane Hospital, which is very much the same, namely about 3 to 4 per cent cesarean sections in the ward cases.

I entirely agree with all that Dr. Aldridge has said and what Dr. Barrett has said in regard to the prevention of mortality in these cases. We are very likely to believe that cesarean section must be rushed, and as a result we do not take enough time and enough trouble in the preparation of our patients prior to operation.

DR. ALFRED C. BECK.—The general idea that most of us hold is that the mortality from cesarean section ought not to be over 1 per cent, if the right operation is done on the right patient at the right time. We pay too much attention to indications and too little attention to contraindications. If we look over the bad results in the Woman's Hospital series, few as they were, we shall find that cesarean section was definitely contraindicated in certain of them, in that the operation was done after the time when cesarean section no longer should have been done.

DR. WILLIAM E. STUDDIFORD.—In looking up the incidence of sections on the Bellevue service I found it amounted to a little over 2 per cent. I do not think we have had any marked fetal mortality as a result of this because our mortality in term infants year after year has run about 3 per cent. Our total maternal mortality

has varied between 0.3 and 0.4 per cent. I do not believe this would have been influenced much by increasing the number of cesarean sections.

In the past five years we have done about 215 sections at Bellevue Hospital, including a considerable number of hysterotomies on toxic patients in whom no improvement had been seen after conservative treatment. The mortality in this group amounted to 3.2 per cent.

One of the striking things in Dr. Barrett's presentation was the very high percentage of cesarean sections for cervical dystocia. I believe there were 225 of them. That amounts to about one-fourth of the indications for cesarean section.

DR. BARRETT (closing).—To Dr. Beck I would say that I believe our incidence was high and that our mortality was too high. If you follow the table, you will find our mortality rate has come down very materially in the last five years. If we could take that selective group which we consider done at the right time, we would have only 1 per cent. It is when we misjudge the case that we get into trouble.

Dr. Studdiford mentioned the high incidence of cervical dystocia. I expected that comment. Cervical dystocia was, however, not the only reason for doing cesarean section in these cases. There are many patients who have disproportion and progress very slowly in labor because of malposition or high occipitoposterior position, who do not engage well and who after a long period of labor have an undilated cervix. These we have come to regard, both in the ward and in the private group, as cervical dystocia.

RETRODISPLACEMENTS OF THE POST-PARTUM UTERUS

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THE use of the knee-chest position for the prevention of retrodisplacement of the post-partum uterus is advocated by almost all writers on the subject. It had always appealed to me as a very rational and valuable procedure. In 1932, however, Schauffler¹ reported a series of cases in which it seemed to have had a deleterious effect. Forty-seven and two-tenths per cent of patients who had done the knee-chest exercises had retrodisplacement of the uterus when examined six weeks post partum while only 34.5 per cent of those who had not done the exercises had retrodisplaced uteri. More recently Eichner² found 22.7 per cent of retrodisplacements among patients who had done knee-chest exercises as contrasted with 27.7 per cent retrodisplacements among those who had not done the exercise.

A favorable opportunity to investigate the problem was provided at the Florence Crittenton Maternity Home, through the kindness of Dr. Thomas R. Goethals and the members of the staff of the hospital. The girls at the hospital remain there for at least six weeks after delivery. As they do their knee-chest exercises under supervision one may be sure the exercises were actually done and done correctly. (One of my patients once told me that I must have a beautiful faith in human nature if I thought that anyone actually did the exercises after she went home.) The statistics herein presented refer to a group of 210 girls who actually did the knee-chest exercises under supervision from ten days after delivery until their discharge examination six weeks post partum. A control series of 210 Crittenton patients

who did not do the knee-chest exercises were likewise examined six weeks post partum. The results are shown as follows:

TABLE I. PATIENTS WITH KNEE-CHEST POSITION
210 Cases Examined Six Weeks Post Partum for Retrodisplacements

	ANTERIOR	RETRODISPLACEMENTS				TOTAL
		1ST DEG.	2ND DEG.	3RD DEG.	UNCLASSIFIED	
No. of cases	136*	5	23	38	8	74
Per cent	64.7	2.4	10.9	17	3.8	35.2

*Includes 5 anteфлекed, 5 good and 2 fair.

TABLE II. PATIENTS WITHOUT KNEE-CHEST POSITION
210 Cases Examined Six Weeks Post Partum for Retrodisplacements

	ANTERIOR	RETRODISPLACEMENTS				TOTAL
		1ST DEG.	2ND DEG.	3RD DEG.		
No. of cases	136	12	28	34		74
Per cent	64.7	5.7	13.3	16.1		35.2

The total number of retrodisplacements was exactly the same in both series. No significant variation appears in the degree of retrodisplacement. This seems to demonstrate that the knee-chest position is completely ineffectual in the prevention of retrodisplacement of the post-partum uterus.

I was unable to learn from what source the use of knee-chest position originally came. I suspect that it is one of those ideas handed down from generation to generation without ever being subjected to statistical study. It was used by Camper in the middle of the seventeenth century and by Deventer in 1701. Von Ritgen in 1820 also used it. The literature of sixty to seventy years ago is filled with debates on the mechanism by which it functions, the influence of air entering the vagina being stressed in several lengthy and highly technical papers. The knee-chest, knee-elbow and other variations of the posture are described. Apparently before the days of aseptic surgery, the knee-chest position was widely used in all types of retrodisplacements. I was unable to discover who first popularized its use in the puerperal state. That it is widely used for the prevention of post-partum retrodisplacements will, I think, be admitted by all, but statistical vindication of the practice seems to be entirely lacking.

A further check was provided by the study of 200 private cases. These patients were all instructed to assume the knee-chest position for ten minutes twice a day. The exercises were started ten days post partum. At the discharge examination from the hospital (usually

TABLE III. TWO HUNDRED PRIVATE PATIENTS SIX WEEKS POST PARTUM

	ANTERIOR	RETRODISPLACEMENTS				TOTAL
		1ST DEG.	2ND DEG.	3RD DEG.		
No. of cases	140	14	14	32		60
Per cent	70	7	7	16		30

fourteen days post partum) any retrodisplacements were corrected but no other treatment was given before the six weeks' examination.

There are 5 per cent less retroversions in this group than in the Crittenton series. The slightly better showing may not be at all significant. If the knee-chest position were effective, the series of Crittenton patients who did the exercises under supervision should show better results than these patients, many of whom were admittedly lax in their performance of the exercise at home. If any difference is shown it is probably due to the correction of retrodisplacements at the discharge examination fourteen days post partum and not to any difference in the method of using the knee-chest position.

An effort was made to determine the influence of parity on post-partum retrodisplacements. As all of the Crittenton patients were primiparas, 100 multiparas and 100 primiparas were chosen from my own cases. The results of their examination at six weeks and six months is tabulated below.

TABLE IV

	ANTERIOR	RETRODISPLACEMENTS			
		1ST DEG.	2ND DEG.	3RD DEG.	ALL RET.
<i>One Hundred Private Primiparas</i>					
6 Weeks	72	8	7	13	28%
6 Months	87	3	2	8	13%
<i>One Hundred Private Multiparas</i>					
6 Weeks	68	6	7	19	32%
6 Months	86	5	2	7	14%

Although no really significant difference appears, it would seem that multiparas are slightly more susceptible to post-partum retrodisplacement. One may surmise that this is due to the greater degree of relaxation found in multiparas. It is really surprising that a greater difference was not found.

It will be noticed that the six months' examination shows over a 50 per cent reduction in the number of retrodisplacements. This was obtained by the use of repeated replacements, pessaries and the knee-chest position. Contrary to the findings of Findlay³ who reported that pessaries cured 75 per cent of retrodisplacements in primiparas and only 38 per cent in multiparas, the multiparas in this series seem equally amenable to treatment. All of the retrodisplacements at this time were apparently symptomless and were not treated further. Grouping the primiparas and multiparas, the following figures are obtained, showing the results at the end of six months.

TABLE V. TWO HUNDRED PRIVATE PATIENTS SIX MONTHS POST PARTUM

	ANTERIOR	RETRODISPLACEMENTS			
		1ST DEG.	2ND DEG.	3RD DEG.	TOTAL RETRO.
No. of cases	173	8	4	15	37
Per cent	86.5	4	2	7.5	13.5

This figure is well below the incidence to be expected in nulliparous women for both Polak⁴ and Stacy,⁵ independently and in large series of cases, have found that retrodisplacements occur in about 20 per cent of nulliparas. It is interesting to compare these figures with others gleaned from the literature.

TABLE VI. INCIDENCE OF RETRODISPLACEMENTS

AUTHOR	TIME POST PARTUM	NO. CASES	UNTREATED	TREATED
Beck ⁶	-----	60	45.0%	
Beck ⁶	-----	37	-----	13.5%*
Danforth and Galloway ⁷	8 wk.	1,000	-----	14.4%†
Eichner ²	6 wk.	191	27.7%	-----
Eichner ²	6 wk.	211	-----	22.7%‡
Findlay ⁸	-----	165	26.6%	-----
Key ⁹	13 wk.	100	33.0%	8.0%†
Litzenberg ¹⁰	6 wk.	-----	25.0%	2.5%†
Lynch ¹¹	1 yr.	1,230	41.4%	-----
Miller ¹²	6 wk.	1,000	22.0%	-----
Moses	6 wk.	210	35.2%	-----
Moses	6 wk.	210	-----	35.2%†
Moses	6 wk.	200	-----	30.0%†
Moses	6 mo.	200	-----	13.5%†
Polak ¹³	-----	-----	35.0%	3.0%§
Schauffler ¹	6 wk.	84	34.5%	-----
Schauffler ¹	6 wk.	84	-----	47.2%†

*Treated by monkey walk, and exercises on all fours.

†Treated by replacement and pessary.

‡Treated by knee-chest position.

§Treated by mule kick.

Although at first sight there may seem to be considerable variation in these series, by taking averages we can arrive at some reliable and confirmatory figures. There is a total of 3,040 untreated cases and the percentage of retrodisplacements figures out as 32.8 per cent. Two percentages are reported without giving the number of cases involved and these average 30 per cent.

The treated cases arrange themselves in three groups. Two authors speak of 3 per cent and 2.5 per cent retrodisplacements.

Dr. Polak's figures are taken from a discussion and Dr. Litzenberg's are obtained from his statement that 25 per cent of post-partum patients have retroversions and that 90 per cent of these may be corrected. Neither statement is supported by accurate figures and perhaps neither was intended to be taken as more than an estimate. Beck found 13.5 per cent retrodisplacements in his patients following monkey walk exercises and in two series replacement and pessary treatment left about 14 per cent of retrodisplacements. In the remainder, the knee-chest position used in a total of 705 cases gave a 32.2 per cent incidence of retrodisplacements, about the same as the incidence of retroversions in untreated cases. Comparison with the results of other forms of treatment serves to re-emphasize the futility of the knee-chest exercises.

From these figures, however, some very interesting conclusions may be drawn. The average percentage of retroversions found post partum in the absence of treatment is 32 per cent, well above the 20 per cent incidence in nulliparous women. Hence pregnancy results in a definite increase in the incidence of retrodisplacements of the uterus. The number of retrodisplacements persisting after treatment,

however, is from 3 to 14 per cent, definitely lower than the percentage of congenital retrodisplacements. Repeated replacement, pessaries, and perhaps exercise on all fours will afford the effective methods of treatment. The facts seem to demonstrate that the uterus is in a rather plastic state as involution progresses and that, by and large, it tends to remain in the position in which it is held while it is shrinking. Therefore unless adhesions are present, even congenital retrodisplacements may be corrected during the process of involution. While many retrodisplacements are symptomless, unless the cure is so difficult as to be worse than the disease, it is worth while to seize the opportunity of restoring the uterus to its normal position.

CONCLUSIONS

1. The knee-chest position is of no value in the prevention of post-partum retrodisplacements of the uterus.
2. Multiparas are little if any more prone to retrodisplacements of the post-partum uterus than primiparas.
3. Unless treatment is given, pregnancy increases the percentage of retrodisplacements found.
4. The plasticity of the pelvic organs, while the uterus is shrinking down after pregnancy, affords an opportunity for correcting retrodisplacements of the uterus including those of congenital origin.

REFERENCES

- (1) *Schauffler*: J. A. M. A. **99**: 726, 1932. (2) *Eichner*: Ohio State M. J. **33**: 1233, 1937. (3) *Findlay, W. M.*: Am. J. Surg. **33**: 546, 1936. (4) *Polak, J. O.*: New York M. J. **111**: 89, 1920. (5) *Stacy, Leda J.*: J. A. M. A. **79**: 793, 1922. (6) *Beck, A. C.*: Am. J. Obst. & Dis. Wom. & Child. **74**: 75, 1916. (7) *Danforth and Galloway*: J. A. M. A. **87**: 826, 1926. (8) *Findlay, W. M.*: AM. J. OBST. & GYNEC. **26**: 874, 1933. (9) *Key*: Texas State M. J. **31**: 715, 1936. (10) *Litzenberg*: J. A. M. A. **99**: 1741, 1932. (11) *Lynch, F. W.*: AM. J. OBST. & GYNEC. **4**: 362, 1922. (12) *Miller, H. A.*: J. A. M. A. **87**: 830, 1926. (13) *Polak, J. O.*: J. A. M. A. **87**: 830, 1926.

Repetti, Mario: Stimuli Which Influence the Secretory Activity of the Mammary Glands, Folia Gynaec.-demograph. 33: 503, 1936.

Folliculin determines the proliferation of epithelial glandular tissue but not the amount of milk secreted. If administered in large doses in the puerperium it inhibits milk secretion.

Corpus luteum and suprarenal cortex hormone do not have a direct or appreciable influence upon the mammary gland.

The thyroid gland although not of great importance is not entirely excluded from the mechanism of lactation. It works indirectly through the hypophysis.

Decidual extract definitely influences the secretory process of the mammary gland, but its action is only partial and probably reflexly acts on the hypophysis, because the mammary secretion is established when the decidua is expelled.

The anterior hypophysis determines proliferation and secretion of the mammary gland; it contains the hormone of lactation, prolactin. The test of Riddle is specific for the hormones of lactation.

MARIO A. CASTALLO

THE RETAINED CERVICAL STUMP*

WITH SPECIAL REFERENCE TO NONMALIGNANT CHANGES

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THE many discussions and the innumerable articles pertaining to the cervical stump revolve chiefly about the possibility of malignancy and about the value of total versus the subtotal hysterectomy, little attention being paid to the fate of the cervical stump that does not develop carcinoma. Gynecologists are prone to spend much time treating the many abnormalities of the cervix before the removal of the corpus, but to lose interest when only the stump remains, unless of course, evidence of malignant changes can be demonstrated. My attention was first drawn to the so-called normal cervical stump when a difference in the iodine absorption (Schiller's test) was noted before and following the removal of the corpus. Biopsy studies are naturally of little value in such cases because of the concomitant trauma to the neighboring tissue. It was possible to demonstrate a noticeable difference in the consistency of the vaginal portion of the cervix before and following the subtotal hysterectomy. The alteration in the vascularity of the retained cervixes, together with the loss of the changes in diameter of the cervical canal which normally accompany menstruation, tend to stricture formation, with subsequent cervical pyometria. These strictures and abscesses are often overlooked in routine examination, especially when the portio vaginalis presents a grossly normal smooth surface and a small external os. Not infrequently it is this type of cervix that constitutes the causative source of backaches, urinary symptoms and a persistent leucorrheal discharge. Simple dilatation of the cervical canal usually results in quick relief.

During a recent clinical and pathologic survey of carcinoma of the cervix, occurring in the Gynecological Service of the Johns Hopkins Hospital between the years 1893 and 1935, I was impressed with the relative paucity of true stump carcinoma following subtotal hysterectomy. In this period of forty-two years, 4,300 uteri were removed subtotally because of myomas and 2,250 for other causes of a benign nature. In this series of 6,550 stumps, we have records of 157 patients returning because of complaints relative to the stump. Of the 157 patients, twenty-six were found to have primary carcinoma of the stump. This figure would be nearly tripled if we included those cases in which cancer was found either at the time of hysterectomy or within the period of one year following the surgery.

*Presented at a meeting of the Section of Gynecology and Obstetrics of the California State Medical Association, May, 1937.

Data from the Gynecological Department of the Johns Hopkins University.

There has been no definite attempt to follow these patients and the data for the most part have been taken from the case reports, so that our figures are relative rather than factual. Many of the statistical reports giving the incidence of stump cancer have been obtained by

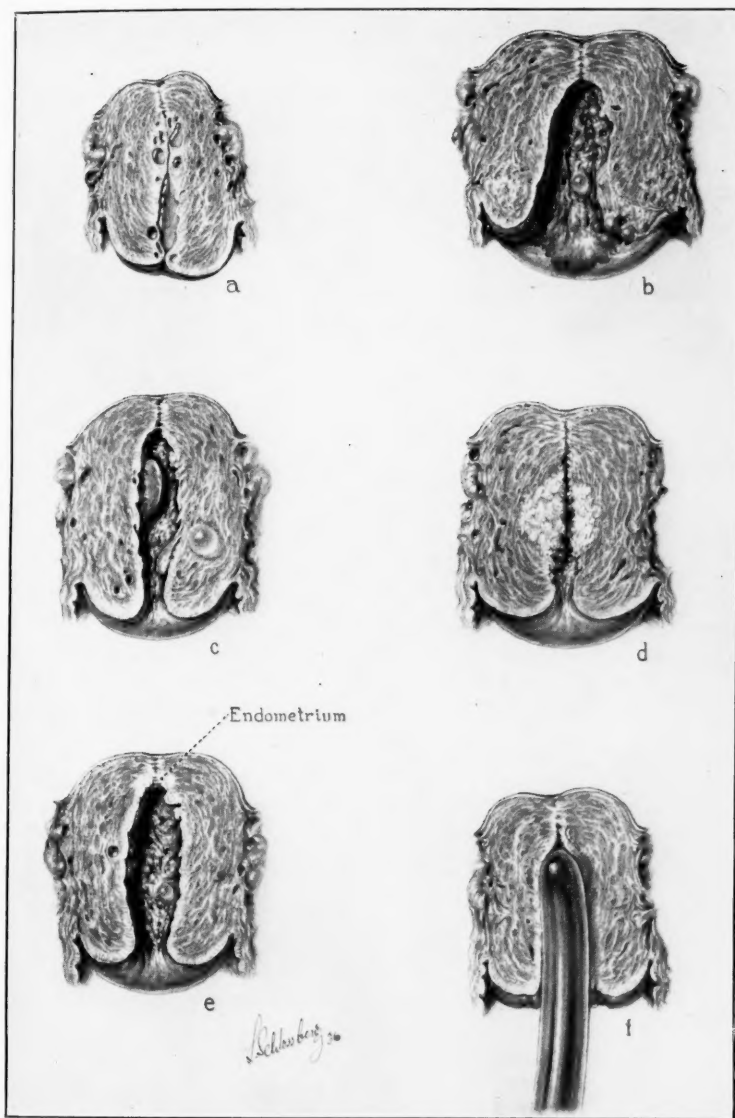


Fig. 1.—*a*, Cervical stump eight years after subtotal hysterectomy showing stricture of the external os with abscess formation in the walls of the canal. *b*, Large hypertrophic cervical stump with so-called erosion of the mucosal elements; there is also a marked inflammatory process. *c*, Two cervical polyps; the one near the os is polypoid in type while the larger growth is flat with a wide base. The cyst on the cut surface is a dilated infected cervical gland. *d*, Cervical stump nine years after subtotal hysterectomy, showing a relatively early intracervical carcinoma of squamous-cell type. *e*, Cervical stump with small islands of functioning endometrium at the apex of the canal. *f*, A No. 9 Hegar dilator introduced into the stump pictured in *a*; providing adequate drainage will frequently clear up these abscesses.

studying series of cases of cervical cancer; this certainly does not express the true incidence. Thus, instead of the 2 to 5 per cent usually cited, our apparent incidence of cervical stump cancer is 0.45 per cent.

While we cannot belittle the importance of the possible later appearance of malignancy in the retained stump, we do feel that the "forgotten stump," the stump that does not show malignant changes, should receive more of our attention. In this series of 6,550 cases, 131 women presented themselves and were admitted to the service because of symptoms arising from benign changes in the cervical stump. Obviously we can give no figures of the many women following subtotal hysterectomy who might have suffered from symptoms referable to a diseased stump and who did not present themselves for assistance.

The following lists the primary complaints impelling patients in this series to seek medical assistance:

	BENIGN	WITH CANCER
Periodic vaginal bleeding	75	1
Irregular vaginal bleeding	22	7
Vaginal discharge, odorless	32	3
Vaginal discharge, offensive odor	19	6
Vaginal discharge, with bleeding	20	9
Prolapsus of the stump	3	0
Urinary symptoms	4	0
	<hr/> 157	<hr/> 26

Periodic Vaginal Bleeding.—The common cause of periodic vaginal bleeding following subtotal hysterectomy is high amputation of the corpus, and the bleeding is therefore an indication of menstrual activity. Most of these patients returned because they had been told they would not menstruate following the operation. The bleeding was always scant and rarely lasted for more than a day. In each instance dilatation and curettage of the cervical canal was done, and in 52 of the cases evidence of retained functional endometrium was demonstrated. It is therefore important that patients with this type of bleeding be carefully instructed as to further possibilities, especially as regards menstrual cycle changes. Four of the 57 cases were found to have an associated endometriosis of the portio vaginalis of the cervix and were treated with the actual cautery. One patient returning twenty-two months following the operation was found to have an adenocarcinoma of the stump. Careful re-examination of the removed corpus failed to disclose any evidence of malignancy that had been overlooked previously. This patient stated that she had experienced a regular scant period each month following the removal of the corpus. She returned because her periods had become increasingly profuse for the past three months.

Irregular Vaginal Bleeding.—Of the 22 patients presenting this complaint, seven had definite malignancy of the stump. We feel that this is the most dangerous group in the series. Patients are not infrequently advised not to be alarmed if they experience scant bleeding on several occasions following the subtotal hysterectomy. Naturally, the patient is likely to interpret such bleeding when it does occur as of no importance. Again, not infrequently abnormal bleeding may even appear several years following the operation and may then be considered as an indication of the menopause. The patients in this group in whom benign lesions were found, presented for the most part, functioning endometrium in association with chronic infections of the cervix or cervical polyps and were treated by cervical cauterization.

Odorless Vaginal Discharge.—Of the 32 patients complaining of an inoffensive vaginal discharge, varying in amount from a self-termed "moderate" to "profuse,"

3 had cancer of the stump. During the past five years, 2 patients who have been examined showed the presence of *Trichomonas vaginalis* infection and responded to specific therapy seemingly more readily than those patients in whom there was a normal menstrual cycle. Twelve of the series were relieved by simple dilatation of the canal and in 8 of these patients retained secretion above the stricture of the external os was demonstrated; the remaining 15 patients were cauterized following the routine dilatation and curettage of the canal.

Offensive Vaginal Discharge.—In this group, 6 of the 19 patients presenting a foul discharge and no evidence of bleeding were found to have cancer. Most of them returned to the hospital complaining of the foul odor and not because of the discharge per se. Four were found to have endocervical polyps, and in 2 patients, definite stricture of the external os with abscess formation was demonstrated.

Vaginal Discharge With Spotting.—There were 20 patients complaining of vaginal discharge with various degrees of bleeding; 9 of these had cancer of the cervical stump. One had endometriosis of the posterior vaginal fornix and an associated marked cervicitis. Cervical polyps were present in two instances, and a small endometrial polyp was demonstrated in one patient. In the cases showing malignant changes in the cervical stump, the average time elapsing between the onset of the bleeding and the patient's appearance for aid was six months; this corresponds closely with the period of delay in cervical carcinoma cases in general.

Prolapsus of the Stump.—We have records of three such instances. Oddly enough 2 of these patients were in their early twenties, the uteri having been removed for lesions other than myomatous involvement. In each instance the stump was suspended by ventroabdominal fixation.

Urinary Symptoms.—Though urinary complaints are not uncommon following either the total or subtotal operation, only 4 patients presented themselves with symptoms of urinary tract irritation that were not alleviated by urinary tract antiseptics, cystoscopy, or topical applications of drugs to the urethra and trigone. In each instance, there was evidence of upper urinary tract irritation with negative bladder cultures. Though topical applications of drugs and bladder instillations gave temporary relief, it was not until the badly infected cervixes were properly treated by the cautery that the urinary symptoms were permanently relieved.

The routine instructions to all the public ward patients at the Johns Hopkins Hospital following any type of operation is to return to the outpatient department at the end of six weeks and again at the end of the first year. At each examination careful note is made of the cervix. If, when examined in the outpatient department, the history or the examination suggests any unusual change in the cervical stump, the patient is admitted to the wards. The cervix is well exposed and the canal is dilated and curetted. If the gross appearance of the obtained tissue does not suggest malignant change, the cervix is then cauterized. If the pathologic report shows malignancy, radiation is immediately instituted. The most frequent pathologic finding is chronic inflammatory tissue and "metaplastic" epithelial changes are not infrequent. Though no statistics are available it is my impression that metaplasia or epidermidization is more frequent in cervical stumps than in other cervixes. Many of these patients who complain of leucorrheal discharge in the absence of cancer show definite evidence of stricture about the external os, in spite of the presence of deep lacerations. We have treated these strictures by dilating the canal to the size of a No. 12 Hegar dilator, generally this is more efficacious than the cautery, but care must be taken not to tear the cervix during the insertion of the dilators. Another adjunct in the examination of the

residual cervical stump, especially in office practice, is the suction curette; this is easily inserted into the canal and, if endocervical malignancy is present, tissue is more readily obtained than follows the use of the usual biopsy forceps.

No article on the cervical stump would be complete without at least some comment upon the problem of the relative advantages of subtotal versus total hysterectomy, as a routine procedure. Our comment, or rather our plea, is directed to the occasional operator rather than to the trained specialist. The time is past when surgery is confined to medical centers with highly trained staffs. We feel that the authors who have and are still debating the value of the two operations have missed the point. It is possible that in the hands of the highly trained specialist there is little difference in the morbidity and mortality rates of the two operations, but in the hands of the less expert surgeon with his operating staff of untrained assistants, the rates do vary to a marked degree. The man in the small community derives his ideas of advancement in technique from the publications of expert gynecologists and with his limited facilities has little opportunity to prove or disprove what he reads. To use the now common term, he is the "forgotten man," and it is for his benefit and to suit his circumstances that suggestions should be made more frequently than they are.

The fact that only 2.4 per cent (157 patients) of our 6,550 patients returned to the hospital with complications referable to the stump, and that of these, we have records of only 26 or a percentage of 0.45 showing cancer, indicates that the incidence of stump cancer is so low as to be of relatively little import. There is no evidence that subtotal hysterectomy predisposes to cancer of the stump or that the residual stump is more susceptible to malignant changes than the cervix of a complete uterus. We do not feel that the 0.45 per cent incidence of stump cancer is sufficient reason to advise the total operation with its morbidity-mortality rate of 2 to 5 per cent. It is common knowledge that in the hands of the less experienced surgeon, total hysterectomy is accompanied with greater risk than when the more conservative operation is employed. The more rational approach would be to fit the operation to the patient and to the physical findings, rather than to advocate either operation as a routine. In considering the choice of operation, one must take into account the surgical ability of the operator and the condition of the patient as well as the possibility of later development of cancer of the stump. With proper pre- and post-operative treatment of the cervix, total hysterectomy merely as a prophylactic against cancer of the stump is probably rarely indicated.

SUMMARY

1. An endeavor has been made to show that the incidence of cancer of the cervical stump is exceedingly low, when studied from the standpoint of its occurrence in a series of subtotal hysterectomy cases, rather than its occurrence in a series of cases of cervical cancer alone.

2. We have the records of 157 patients out of 6,550 subtotal hysterectomy cases presenting themselves with symptoms referable to the stump and have classified them according to their complaints.

3. In the hands of those who are not expert in pelvic surgery, total hysterectomy is a more dangerous procedure than the more conservative subtotal operation. The exceedingly low incidence of stump cancer is not sufficient reason to advocate the routine use of the total operation. The ideal procedure in most cases consists of proper conservative care of the cervix before removing the corpus, followed by periodic examinations of the stump after operation.

523 WEST SIXTH STREET

THE EFFECT OF PROGESTIN UPON THE ANTERIOR PITUITARY

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IT IS undesirable and dangerous to draw inferences from the results of experimental work in one species and to expect these inferences to hold true in detail in another. Basic physiologic principles, however, usually carry over from species to species, in a modified form at least.

Progestin, one of the ovarian hormones secreted by the corpus luteum, exerts an effect upon two components of the uterus, the muscle and the endometrium. The endometrium is changed from the proliferative stage to the secretory or progestational type in both the rabbit¹ and the human being.² The hormone inhibits the normal response of the uterine muscle of the rabbit to extracts of the posterior pituitary.^{3, 4} Similar action in the human being is reported,⁵⁻⁷ although other investigators cannot confirm the finding.⁸⁻¹⁰ Thus we see that the action of progestin upon the endometrium in both rabbit and man is similar, as is possibly also its action upon the uterine muscle.

It has been known for many years that rabbits in heat will mate and ovulate ten to twelve hours later.¹¹ It has also been common knowledge that rabbits mate during pregnancy and pseudopregnancy, but never ovulate following these matings.¹¹ During pregnancy and pseudopregnancy there are present in the ovary functional corpora lutea, and it was generally acknowledged that these glands probably played a part in suppressing ovulation; the mechanism of the action remained, however, obscure.

Pseudopregnancy might be described at this time for those unfamiliar with the reproductive mechanism in the rabbit. Rabbits ovulate only after sexual stimulation of some sort, the natural and commonest one being copulation. A doe mated with

a vasectomized buck ovulates, corpora lutea form, but since there are no sperm in the female generative tract, the ova are not fertilized. The corpora lutea so formed are functional and normally do not begin to degenerate until the fifteenth or sixteenth day after mating. This sixteen-day period is generally termed pseudopregnancy.

In attempting to demonstrate the active factor responsible for this suppression of ovulation in the rabbit, it was first shown that a change in sensitivity of the ovarian follicle to gonadotropic material was not the reason for the failure. On the eighth day of pseudopregnancy, only one-third more gonadotropic material was necessary to cause ovulation than was the required dose for a rabbit in heat.¹² The pituitaries of these eight-day pseudopregnant animals were known to contain many times more activity than was represented by the minimal effective dose administered.¹³ The conclusion was reached, therefore, first that the follicles could and would ovulate if essentially normal amounts of gonadotropic material were released to the blood stream and second, that ample material to cause ovulation was contained in the anterior pituitary gland.

Interest was next directed toward the hormonal status of the anterior pituitary of the rabbit during pseudopregnancy, both before and after coitus.

The gonadotropic content of the pituitary gland on the eighth day of pseudopregnancy was examined both before and after coitus in order to determine the effect, upon the pituitary, of copulation during the active life of the corpora lutea. As controls, pituitaries of estrous (post partum) rabbits were taken and also of rabbits twenty-four hours after a mating which had been shown to have resulted in ovulation. The results in summary form are as follows: The gonadotropic content of the estrous glands was approximately 25 Rb. U. Twenty-four hours after a mating which resulted in ovulation, the pituitary contained 5 Rb. U. or less. Therefore, normally in estrous animals as a result of the stimulus of coitus, there is a nearly complete discharge of the gland. At the eighth day of pseudopregnancy, the gonadotropic content of the pituitary has been restored to at least the estrous level.^{13, 14} However, when these pseudopregnant rabbits accept the buck and their pituitaries are removed twenty-four hours later, it is found that there has been insufficient discharge of gonadotropic material to be detected.¹⁵ Consequently, during pseudopregnancy and presumably pregnancy, ovulation does not occur because the normal discharge of gonadotropic material from the pituitary following coitus is in some way inhibited.

The next step in the problem was to investigate the effect of progestin upon the pituitary. Progestin in doses of 2 Rb. U. or progesterone, the pure crystalline hormone, in doses of 2 mg. given daily for five days to estrous rabbits was found to inhibit ovulation normally following coitus.¹⁶ No rabbit, after taking the buck, ever ovulated when receiving this or a larger dose. When the pituitaries of these mated animals receiving corpus luteum hormone were compared, as to gonadotropic content, to those of identically treated un-

mated animals taken as controls, it was found that there had been no detectable discharge of gonadotropic material from the glands.¹⁷

These results seem conclusive and permit one to state that pregnant and pseudopregnant rabbits do not ovulate because functional corpora lutea in their ovaries, by secreting progestin, prevent discharge of the gonadotropic content of the pituitary. Neither the mode nor yet the site of action of the hormone is explained by these results. It could conceivably act in any of several ways; one, by preventing the stimulus of coitus from reaching the pituitary or two, by preventing the discharge of the material into the blood stream, presuming the stimulus to have arrived, or three, by still some other action of which we have at present no clue. Experiments to demonstrate these unknown factors will have to be devised and carried out and also additional experiments planned to show whether or not one is correct in anticipating that progestin, in the human being, will be found to have a definite action upon the anterior pituitary gland similar in general to that which has been demonstrated to be true in the rabbit.

REFERENCES

- (1) Corner, G. W., and Allen, W. M.: *Am. J. Physiol.* **88**: 326, 1929. (2) Kaufmann, C.: *Zentralbl. f. Gynäk.* **56**: 2058, 1932. (3) Knaus, H.: *Arch. f. exper. Path. u. Pharmacol.* **151**: 371, 1930. (4) Makepeace, A. W., Corner, G. W., and Allen, W. M.: *Am. J. Physiol.* **115**: 376, 1936. (5) Knaus, H.: *Zentralbl. f. Gynäk.* **53**: 2193, 1929. (6) Knaus, H.: *Ibid.* **57**: 2658, 1933. (7) Hermstein, A.: *Arch. f. Gynäk.* **144**: 500, 1931. (8) Moir, J. C.: *Tr. Edinburgh Obst. Soc.* **54**: 93, 1934. (9) Robertson, E. M.: *Edinburgh Med. J.* **44**: 20, 1937. (10) Kurzrok, R., Wiesbader, H., Mulinos, M. G., and Watson, B. P.: *Endocrinology* **21**: 335, 1937. (11) Hammond, J., and Marshall, F. H. A.: *Reproduction in the Rabbit*, Edinburgh, 1925. (12) Weinstein, G. L., and Makepeace, A. W.: *Am. J. Physiol.* **119**: 508, 1937. (13) Hill, R. T.: *J. Physiol.* **83**: 129, 1934. (14) Friedman, M. H.: To be published. (15) Makepeace, A. W., Weinstein, G. L., and Friedman, M. H.: *Endocrinology* **22**: 667, 1938. (16) Makepeace, A. W., Weinstein, G. L., and Friedman, M. H.: *Am. J. Physiol.* **119**: 512, 1937. (17) Makepeace, A. W.: To be published.

Rorke, Margaret: **Gonorrhea in Women and Children**, *Lancet* **1**: 932, 1938.

The author reviews the signs and symptoms of gonorrhea in women and children. The frequency of rectal infection is noted, and the necessity of rectal examination during the treatment of every case is emphasized.

Treatment advised by the author consists of rest, douches in the presence of profuse discharge, topical applications and the administration of prontosil album in 3.5 to 4 gm. daily doses for seven days, if tolerated, followed by one-half this amount daily for another week. The use of heat therapy with the Elliott machine is recommended in pelvic infection.

In the child local cleanliness, with either estrogenic hormone therapy or prontosil album in 1 or 2 gm. daily doses (given in 4 divided doses), is advised.

The test of cure is described as negative films and cultures immediately following three menstrual periods, the last at least after a month without treatment and following provocative painting of the cervix or alcohol stimulation. The importance of routine cultures is emphasized, as in 323 out of 871 cases studied the films were negative and cultures positive.

CARL P. HUBER

FOOD HABITS OF MOTHERS OF CONGENITALLY MALFORMED CHILDREN

REPORT OF 545 FAMILIES

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CERTAIN characteristics of a series of families, each of which had given rise to a congenitally malformed child, were the object of a recent investigation.¹⁻¹² The study was planned to determine if any characteristic of these families might have predisposed to the occurrence of the malformations in the offspring. Advanced parental age was found to be such a predisposing factor, because the older couples gave rise to malformed children more often than did the younger ones.⁶

The food habits of the mothers likewise were studied with the same idea in mind, an analysis of the data upon this point forming the basis for the present report.

The essential components of an adequate diet during pregnancy indicate that minerals and vitamins should be increased at this time to supply the extra demands made upon the mother by the fetus (Table I). To accomplish this, in terms of foods, the following changes are usually made from the normal diet:

BASIC FOODS FOR THE NORMAL DIET OF ADULT WOMEN USE DAILY	BASIC FOODS FOR THE DIET DURING PREG- NANCY USE DAILY
1 pint milk	1 quart milk
1 to 2 servings leafy vegetables	2 to 3 servings leafy vegetables
2 to 3 servings other vegetables	2 to 3 servings other vegetables
1 to 2 servings fruit	3 to 4 servings fruit (1 or 2 servings citrus fruit)
3 slices bread	3 or more slices bread, whole grain vari- eties preferred
1 serving meat or fish	Meat or fish as recommended by physician
1 egg	1 egg
1 to 2 ounces of butter	1 to 2 ounces of butter
Vitamin concentrates as directed by physician	Cod liver oil or vitamin A, B ₁ , and D con- centrates as directed by physician

MATERIALS AND METHODS

Collection of Data.—There were located in the files of the Bureau of Vital Statistics, Department of Health of the State of Pennsylvania, 130,132 death certificates for stillborn and liveborn individuals who died in Philadelphia during the five years between Jan. 1, 1929, and Dec. 31, 1933. Each of these certificates was examined and among them were found 1,476 cases of congenital defect.

The deceased individual was considered to have possessed an abnormality under either of two conditions: (1) if the malformation involved the surface of the body, or (2) if internal, its presence had been disclosed by operation or necropsy. Diagnoses not conforming to these requirements were considered as not verified and were excluded from further consideration. This procedure gave 890 cases for study.

TABLE I. COMPARISON OF DAILY FOOD REQUIREMENTS* FOR THE NONPREGNANT AND PREGNANT WOMAN

DAILY ESSENTIAL	NONPREGNANT WOMAN	PREGNANT WOMAN
Calories	2,000 to 2,600	2,000 to 2,600 for first 3 months 2,400 to 3,000 for second 3 months Decrease to 2,000 to 2,200 during last 2 months if gain in weight is more than normal
Protein	1 gm. per kilo	1 gm. per kilo during first 3 months 1.5 gm. per kilo during later months
Calcium	0.55 to 0.68 gm. (0.023 gm. per 100 calories)	1.0 to 2.0 gm.
Phosphorus	1.06 to 1.32 gm. (0.044 gm. per 100 calories)	1.5 to 2.0 gm.
Iron	15 mg.	18 to 20 mg.
†Vitamin A	6,000 international units, at least	An increase desirable
†Vitamin B ₁	300 international units	An increase desirable
†Vitamin C	300 international units	An increase desirable
†Vitamin D	400 international units	An increase desirable
†Vitamin G	400 to 600 Sherman-Bourquin units (20 units per 100 calories)	An increase desirable

*See references 13-15.

†See reference 16.

TABLE II. DIAGNOSES OF CHIEF CONGENITAL MALFORMATIONS BY SYSTEM

Showing the distribution of the congenital defects in the offspring of the mothers who answered the food questionnaires, arranged by body system. Each individual is represented by his most serious defect in cases in which two or more malformations were present.

SYSTEM	INDIVIDUALS
Central nervous	383
Gastrointestinal	72
Cardiovascular	51
Skeletal	32
Genitourinary	3
Multiple	3
Respiratory	1
Total	545

The malformed offspring are grouped in Table II according to the diagnosis of the chief defect. The serious nature of the defects is indicated by the fact that approximately 90 per cent of the malformed children were either stillborn or died within a year of birth.

An attempt was made to interview the mother of each defective individual, the visits being carried out in the summer of 1934 by four fourth-year medical students. Each visitor was supplied with a five-page questionnaire, one sheet of which contained the following questions bearing on diet:

1. How much milk do you use daily in any way?
None 1 cup 2 cups 3 cups 4 cups
2. What green vegetables do you like and eat? How often? Once or twice daily? Once or twice weekly?
3. What other vegetables do you like and eat? How often?
4. What fruit do you like and eat? How often?

5. How much bread do you generally eat? ----- slices per meal. What kind of bread?
 6. What foods do you like and eat most often?
 7. How much coffee do you generally drink? ----- cups.
How much tea do you generally drink? ----- cups.
How much beer, wine or other such drinks do you take daily? ----- glasses.
 8. Did you eat about like this when you were pregnant? Yes ----- No -----
- Differences:

RESULTS

Examination of the answers to the food questions revealed considerable variation in the skill and accuracy of recording. After eliminating the questionnaires which were not filled out satisfactorily, 545 were considered suitable for analysis.

FOOD DATA

Milk.—Facts upon the use of milk appear in Table III. Of the 526 women who reported, 40 per cent used none, and of the 60 per cent who used milk, 45 per cent used less than one quart a day.

TABLE III. DAILY CONSUMPTION OF MILK

Showing the usual daily consumption of milk by the mothers of the malformed children. Note the high percentage of mothers (40 per cent) who took no milk.

MILK	MOTHERS	
	NUMBER	PER CENT
None	208	40
Less than 1 quart	241	45
1 quart	72	14
Over 1 quart	5	1
Total	526	100

More women reported increased use of milk than of any other single food. Twenty-four (4.5 per cent), who did not use milk regularly in their diet, reported using more during pregnancy. Thirty-one women (6 per cent) took from 1 pint to 1 quart more milk when pregnant.

Adjusting these figures to those obtained on the regular use of milk, the significant facts about its consumption by this group are: About 35 per cent took no milk during pregnancy, and about 20 per cent took 1 quart or more daily.

In this country, one quart of milk daily is the usual recommendation for the normal expectant mother. It is recognized as the most valuable single food source of calcium and phosphorus in good amounts and good proportions during pregnancy. American mothers who habitually take less than one quart daily are usually on calcium and phosphorus deficient diets. Using a standard of one quart of milk daily, 80 per cent of these mothers were on diets low or deficient in these minerals.

Vegetables.—The use of vegetables was reported upon by 518 women (Tables IV and V). Only 19 women (4 per cent) reported eating more vegetables during

TABLE IV. LEAFY VEGETABLES

Showing the use of leafy vegetables by the mothers of the malformed children. Note the small percentage of mothers who used two or more servings of leafy vegetables daily.

SERVINGS	MOTHERS	
	NUMBER	PER CENT
1 weekly	23	4
2 weekly	89	17
3 or 4 weekly	29	6
1 daily	290	56
2 daily	89	17
3 daily	6	1
Total	518	100

TABLE V. NONLEAFY VEGETABLES

SERVINGS	MOTHERS	
	NUMBER	PER CENT
Less than 1 daily	52	13
1 daily	236	58
2 daily	93	23
3 or 4 daily	24	6
Total	405	100

pregnancy, so the above figures are fairly representative of the amount of vegetables consumed. If two servings of leafy vegetables and two to four servings of other vegetables daily be accepted as a desirable amount during pregnancy, allowing for 4 per cent increased consumption of both kinds of vegetables, only 20 per cent of the mothers ate adequate amounts of leafy vegetables, and only about 10 per cent consumed desirable amounts of the other vegetables.

As vegetables in general, and leafy vegetables in particular, are valuable sources of calcium, phosphorus, iron, roughage, vitamins A and G and also for C, if eaten raw, low amounts in the diet tend to contribute to mineral and vitamin deficiencies.

Fruit.—The use of fruit was reported upon by 467 women (Tables VI and VII).

TABLE VI. FRUIT

SERVINGS	MOTHERS	
	NUMBER	PER CENT
None (or only occasionally)	58	12
Less than 1 daily	94	20
1 daily	255	54
2 daily	43	10
More than 2 daily	17	4
Total	467	100

TABLE VII. CITRUS FRUIT

SERVINGS	MOTHERS	
	NUMBER	PER CENT
None	14	6
Less than 1 daily	122	55
1 daily	74	33
2 daily	13	6
Total	223	100

Thirteen women (2 per cent) reported eating more citrus fruit during pregnancy and 17 women (3 per cent) said they ate more fruits in general. Adding this increase to the figures on the usual intake of fruit, about 18 per cent had citrus fruit once daily and 13 per cent had about two servings of other fruit daily.

Citrus fruit is of special value in the prenatal period for increasing vitamin C in the diet. Its regular use, one to two servings daily, is highly desirable. Citrus as well as other fruits also make valuable contributions to the mineral, vitamin, and laxative properties of the diet. Less than one-fourth of this group reported eating the amounts of fruit usually recommended to expectant mothers.

Bread.—The use of bread was described by 520 women (Table VIII). Five mothers (1 per cent) reported eating less bread, and 5 reported eating more during pregnancy.

The usual suggestion about the use of bread during pregnancy is about two slices per meal. Larger amounts tend to replace the more valuable fruits and vegetables. About 57 per cent of this group reported two slices or less per meal. Approximately 25 per cent used too much bread.

Whole grain breads contain approximately 50 per cent more minerals than white bread, and are a valuable source of vitamin B₁. Their use during reproduction makes a definite contribution to the mineral and vitamin B₁ adequacy of the dietary. Only 17 per cent used whole grain bread regularly or often.

TABLE VIII. BREAD

BREAD SLICES PER MEAL	MOTHERS	
	NUMBER	PER CENT
None or less than 1	47	9
One	94	18
Two	158	30
Three	92	18
Four	71	14
Five	30	6
Six	8	1
More than 6	20	4
Total	520	100

Kind of Food Liked and Eaten Most Often.—This question was asked as a possible means of better understanding food habits and as a check on the other food facts given. The answers are summarized in Table IX. The food preferences as listed

TABLE IX. FOODS EATEN MOST OFTEN AND MOST DESIRED

KIND OF FOOD	NUMBER OF WOMEN
Vegetables	163
Meat	152
Potatoes	146
Cereals	54
Eggs	33
Fruit	23
Fish	17
Soups	15
Bread	9
Sweets	8
Cheese	2

seemed to confirm other dietary facts and include foods which should contribute to a good diet if used in adequate amounts. Economic conditions are a definite factor in determining the type of food eaten most often, for many women listed these foods with the phrase "if I can get it."

Coffee, Tea, and Alcoholic Beverages.—The data on the consumption of coffee, tea, and alcoholic beverages showed no abnormal or excessive use of any of these beverages.

Changes Made in Diet During Pregnancy.—The changes made in the diet during pregnancy are summarized in Table X.

TABLE X. CHANGES MADE IN DIET DURING PREGNANCY

	MOTHERS	
	NUMBER	PER CENT
Mothers reporting	526	100.0
No change in diet	346	65.8
Ate more	24	4.5
Ate less	34	6.4
Drank more milk	24	4.5
1 pt. to 1 qt. more of milk	31	6.0
More vegetables	19	—
More oranges	13	—
Other fruit	17	—
Less meat	12	—
Less bread	5	—
Less vegetables	5	—
More candy	4	—
More condiments	4	—
More potatoes	2	—
More eggs	1	—

Adequacy of Diet.—The present figures show that the protective foods, such as milk, leafy vegetables, fruits, and whole grain breads were present in the diet of these women in amounts too low to meet the mineral and vitamin standards as recommended for expectant mothers, no one of which reported the use of any vitamin concentrate. The most obvious dietary deficiencies were in calcium, phosphorus, iron, vitamins B₁₂, C, and D. As each of these essentials is important for physiologic well-being, especially during pregnancy, the diet of this group of women was obviously far below desirable standards.

Anemia.—Estimations of the hemoglobin made when the patients were pregnant with their malformed offspring were available for 90 (16 per cent) of the 545 mothers. Of these 90 women, 41 (45 per cent) gave hemoglobin estimations of less than 70 per cent of normal. Reid and Mackintosh¹⁷ in a study of 1,000 pregnant women, found only 10 per cent with a similar degree of anemia. Therefore, the mothers of the malformed children presented a frequency of anemia which was four times that found in the series reported by Reid and Mackintosh.

Of the 90 women for whom hemoglobin estimations were available, 37 (41.2 per cent) used an inadequate diet. Of the latter, 23 (62.2 per cent) had hemoglobin estimations of less than 70 per cent of normal. Whereas, of the 53 who used a balanced diet, only 18 (34 per cent) showed an equal degree of anemia. Therefore, anemia was found in association with an inadequate diet nearly twice as frequently as with an adequate one.

No data were available upon the hemoglobin content of the blood of the malformed offspring.

The present report offers no proof that the inadequate diet of the mothers or the associated anemia were predisposing causes to the occurrence of the congenital malformation in their offspring. It would seem to be within the realm of possibility, however, that dietary deficiency might be a predisposing factor.

SUMMARY AND CONCLUSIONS

An attempt was made to obtain dietary facts from mothers who had given birth to children with congenital defects. Accurate quantitative food intake data could not be secured, but efforts were directed toward obtaining facts about the quality and the possible adequacy of the diet. On the basis of generally accepted dietary suggestions for expectant mothers, questions were planned which might be the means of assembling information about the regular food habits of this group of mothers and the changes they made in their diet during pregnancy.

Records from 545 women were studied. An analysis of the dietary data which they gave to the medical examiners showed:

1. About 35 per cent of this group of women took no milk during pregnancy.
2. About 20 per cent took one quart or more daily.
3. About 20 per cent had two servings daily of leafy vegetables and only 10 per cent reported having 2 to 4 servings daily of other vegetables.
4. Eighteen per cent reported using citrus fruit once daily and 13 per cent had about two servings of other fruit daily.
5. About 25 per cent used too much bread and only 17 per cent used whole grain bread regularly or often.
6. Excessive use of coffee, tea, or alcoholic beverages was not indicated by the reports given.
7. Approximately 40 per cent of these women had an inadequate diet when pregnant with their malformed offspring.
8. Among the mothers using an inadequate diet, anemia was found twice as frequently as among those using an adequate diet.

9. Anemia in the women who gave birth to congenitally malformed children was found four times as often as in a control series.

10. The present observations offer no proof that an inadequate diet or anemia are predisposing causes for the occurrence of congenital malformations. It is of interest, however, that both characteristics should have been observed with unusual frequency.

REFERENCES

- (1) *Murphy, D. P., and Mazer, M.*: J. A. M. A. 105: 849, 1935. (2) *Murphy, D. P.*: South. M. J. 29: 79, 1936. (3) *Idem*: AM. J. OBST. & GYNEC. 31: 106, 1936. (4) *Idem*: J. A. M. A. 106: 457, 1936. (5) *Idem*: Surg. Gynec. Obst. 62: 585, 1936. (6) *Idem*: Am. J. Dis. Child. 51: 1007, 1936. (7) *Idem*: Surg. Gynec. Obst. 63: 443, 1936. (8) *Idem*: Ibid. 63: 593, 1936. (9) *Idem*: AM. J. OBST. & GYNEC. 32: 873, 1936. (10) *Idem*: Surg. Gynec. Obst. 64: 646, 1937. (11) *Idem*: AM. J. OBST. & GYNEC. 34: 890, 1937. (12) *Idem*: Ibid. 35: 653, 1938. (13) *Rose, M. S.*: Foundations of Nutrition, ed. 3, New York City, 1938, The Macmillan Co. (14) *Sherman, H. C.*: Chemistry of Food and Nutrition, ed. 4, New York City, 1937, The Macmillan Co. (15) League of Nations Technical Commission of the Health Committee, Report on the Physiological Bases of Nutrition, 1936, League of Nations Publications Department, Geneva. (16) *Eddy, W. H.*: Address before The Philadelphia Dietetic Association, December, 1937. (17) *Reid, W. J. S., and Mackintosh, J. W.*: Lancet 232: 43, 1937.

ANTE-PARTUM RUPTURE OF THE UTERINE SCAR FOLLOWING LOW FLAP CESAREAN SECTION*

WITH A REPORT OF A CASE GIVING RISE TO A SECONDARY
ABDOMINAL PREGNANCY

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THE rupture of a low flap cesarean section scar during a subsequent pregnancy has been reported but infrequently. The subject has not received the attention accorded the same type of accident following classical cesarean sections. It is my purpose to review the subject, and to add a case of such rupture, which is extremely rare as to causation and end result.

For the sake of comparison, some of the historical aspects of uterine rupture following the classical type of cesarean section will be briefly reviewed.

Krukenberg,¹ in 1886, reported 20 cases of rupture of the uterus during pregnancy in patients having had classical cesarean section, and stated that one-half of all cesarean scars ruptured during a subsequent pregnancy, with a 50 per cent mortality in the patients suffering the accident. According to Porro² it was the custom at that time to return the unsutured uterus to the abdominal cavity, with little or no attempt to control hemorrhage. It is not surprising, therefore, to find that Harris,³ in 1878, reported that of 80 cesarean sections done in the United States up to that time, 52.5 per cent of the patients died following the operation. If the figures of Krukenberg and Harris are combined, it becomes apparent that of 100 women having cesarean section at that time, 47 would survive. If these 47 again became pregnant, 24 would have a rupture of their uterus and 12 would die. If it became necessary for the surviving 36 to have a second cesarean section, only 18 of the original 100 patients would survive. This was sixty years ago.

A few years later, in 1882, Sänger⁴ wrote his classical monograph on the proper method of suturing the incised uterus. This was a turning point, for in the following thirteen years he observed 500 consecutive patients who had gone through

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pregnancy following cesarean section without a single case of ruptured uterus. This would be unusual even today, so it might be well to note the fact that he used linen suture material throughout the uterine incision.

Palmer Findley,⁵ in 1916, reviewed the literature from the time of Krukenberg, and found reports of 63 cases of rupture of the pregnant uterus subsequent to a cesarean section. Asa B. Davis,⁶ in 1927, reported 24. La Mariana,⁷ in 1933, brought the total number of cases to 175. We have found 36 others since that time, making a total of 208. Casual conversation in any obstetric group, however, will convince one that this is probably only a small portion of the cases, as many men do not bother to report such a common complication. The percentage of uterine ruptures following classical sections varies from 2 per cent according to Kerr,⁸ to 6 per cent according to Audebert,⁹ but the generally accepted figure seems to be 4 per cent. Holland¹⁰ has further found that 43 per cent of such ruptures take place before the onset of labor, while 57 per cent occur during labor. The estimated mortality varies from 13 per cent according to Asa B. Davis, to 50 per cent according to Weber.¹¹ Our review of several other series indicates a general mortality of about 30 per cent, the rate apparently depending on the availability of hospital facilities.

The statistical background of the cervical or low flap cesarean section presents a slightly different picture. The operation originated after the advent of aseptic surgery, and has been essentially a procedure to be carried out only by the experienced obstetrician. The results have been colored, therefore, by the absence of many of the catastrophes resulting from casual abdominal surgery. The operation as we know it today originated about 1907, and has since undergone numerous modifications.

Wettenwald,¹² in 1926, reviewed 3,600 pregnancies in patients who had a previous low flap cesarean section. Gellé,¹³ in 1932, again reviewed all available cases. Both observers reported that the incidence of rupture of a pregnancy subsequent to this type of procedure was about 0.25 per cent, or 1/16 of that found following the classical type of operation. A painstaking review of several thousand low flap cesarean operations reported since that time have confirmed these findings. The total recorded number of cases of ruptured uterus following low flap cesarean section to date is 36. Of these, only 3 have occurred before the onset of labor. This is less than one-fifth the number rupturing ante partum in the classical cesarean section series. The mortality following rupture is about the same in both types of operations.

In studying these cases of ruptured uterus following the low flap cesarean section, a few predisposing factors seem to stand out. (1) Local infection at the time of previous section, as manifested by foul lochia and a febrile postoperative course, (2) hurried closure of the uterine wound due to the patient's condition, (3) low implantation of the placenta on the uterine wall, over the scar of the previous section.

This latter is the most important and most constant factor, for it was found repeatedly in the cases reviewed. It is reasonable to assume that this is also the explanation of those cases in which a patient delivers spontaneously following a cesarean section and then suffers a ruptured uterus in the third pregnancy. It is being stressed, too, because of its presumptive importance in the case to be reported.

There is another frequent observation which should be emphasized, namely, that in those patients in which the product of conception was completely expelled from the uterus through the site of rupture, hemorrhage was moderate and recovery the rule. Partial expulsion, on the other hand, prevents uterine contraction and may be the direct cause of a fatal hemorrhage. Cameron¹⁴ seems to have been the first to stress the importance of this point.

Practically every case studied brought out the point that rupture of these low flap scars was "silent," or practically symptomless, the accident being discovered only at the time of operation.

Of the three previously reported cases of ante-partum rupture following low flap cesarean section, the most interesting was that of Perez and Talioferro.¹⁵ Briefly, this patient had a separation of the uterine scar early in a pregnancy which followed a low flap cesarean section for placenta previa. A second low flap cesarean section

was performed in the eighth month of gestation, the indication being vaginal hemorrhage. The placenta was found attached to the lower uterine segment anteriorly, with a portion of it growing into the posterior wall of the bladder through the rent in the uterus. The patient died on the table of hemorrhage. Microscopic study of sections from the bladder wall confirmed the gross findings. A fourth case has recently been observed by E. G. Waters.

CASE REPORT

Mrs. E. P., 20 years of age, white, para i, gravida ii, was admitted to Bellevue Hospital with a history of having undergone a low flap cesarean section on the same service one year previously, the indication being a generally contracted pelvis. The operation was done by Hervey C. Williamson under local anesthesia and no difficulty was encountered. The uterus was incised vertically, and the incision limited to the lower uterine segment. Following the delivery of a normal baby, the uterine incision

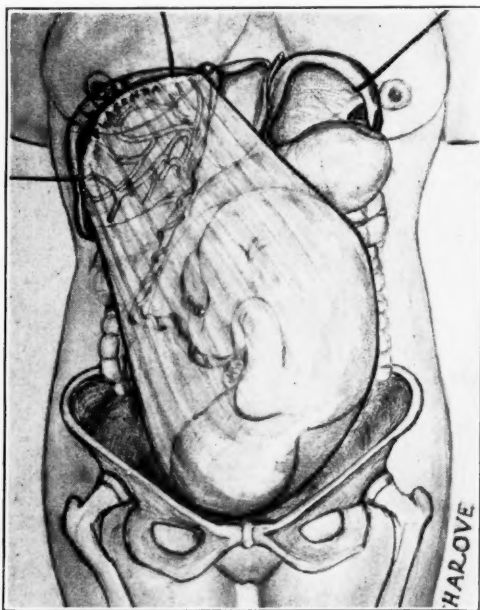


Fig. 1.—The placenta is attached to the right lobe of the liver, and to the gall bladder. The fetus is lying in intact membranes.

was closed in two layers with catgut. The patient had a morbid postoperative course, with foul lochia and some superficial infection of the abdominal wall. This condition cleared up and the patient was discharged as cured on the sixteenth day after operation. Pelvic examination at this time and several weeks later revealed no abnormal findings. Such was the course of her first confinement.

The present, or second pregnancy, began less than a year later, and the patient applied to the clinic, where she was found to have a second normal intrauterine gestation. The pelvis was otherwise negative. Subsequent visits were few and irregularly spaced, due to lack of cooperation from the patient. No complaints were recorded at any of these visits.

The patient's second admission to Bellevue Hospital was four weeks after the expected date of her second confinement. She was admitted complaining of a few mild, cramplike pains in the lower abdomen. No vaginal discharge was present. The fetal heart sounds were heard by the interne, resident, and attending obstetricians. Abdominal examination revealed a large fetus lying in a normal position with the

head floating. All the signs and symptoms of a mild pre-eclamptic toxemia were present. In view of this and the previous cesarean section for pelvic disproportion, no vaginal examination was done. The patient was prepared and sent to the operating room, at which time the fetal heart sounds were again found to be normal. Unfortunately, an emergency call from the ward necessitated delaying the operation for about one and one-half hours. When this emergency had been taken care of, the patient was routinely examined again, but no fetal heart sounds could be heard. It was decided to carry out the operation as planned.

When the abdomen was opened a large fetus was found lying in intact membranes directly within the parietal peritoneum. The membranes were ruptured artificially and the fetus delivered. No heart sounds were present. The fetus was perfectly normal in appearance, no evidence of maceration being observed. It was apparent that death had taken place only a short time before. A placenta of normal size was found intimately adherent to the liver and gall bladder. Removal not being feasible, the placenta was not disturbed except to prove definitely that it was firmly attached. There was no blood in the abdominal cavity. The uterus was found to be

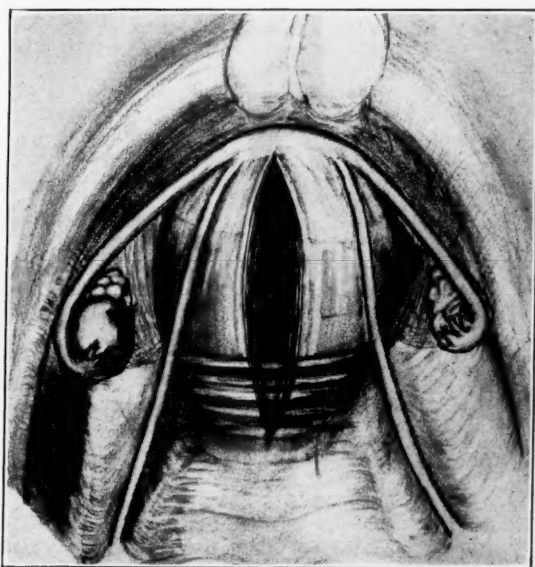


Fig. 2.—Illustrating the extent and location of the rupture of the anterior wall of the uterus.

enlarged to the size of a three months' gestation, with the anterior uterine wall split completely open from the lower angle of the previous low flap cesarean scar to the upper third of the fundus. The edges were everted and dry, so that the rupture was obviously an old one. The operator's fingers were introduced through the rupture into the cavity of the uterus, which was empty. The edges of the ruptured area were freshened with a scalpel and then sutured together with three layers of chromic catgut. The abdomen was closed in layers.

The patient's postoperative course was normal except for profuse drainage from the upper angle of the wound where the umbilical cord had been brought out of the abdominal cavity. This drainage, which resembled degenerated placental tissue, continued for about five weeks, after which the small opening healed spontaneously. Several subsequent examinations, both pelvic and abdominal, failed to reveal any masses.

In questioning the patient again after this second operation, the following history was elicited. The patient had a normal pregnancy until she accidentally fell from a stepladder a distance of some six feet. She struck the floor in a sitting position, arose, and a few minutes later experienced a sharp pain in the lower abdomen. This

was sufficiently severe to force her to go to bed and remain there for four to five days, but not marked enough to cause her to seek medical aid. This, she thought, occurred at the fourth month, but the date could not be definitely ascertained either from the patient or the ante-partum clinical records. Following this she experienced some indefinite abdominal discomfort for several weeks, none of which was referred to the upper abdomen. About six weeks following this accident she returned to the clinic and was examined, but nothing unusual was discovered. Her pregnancy continued in an apparently normal manner, until, as stated before, she voluntarily entered the hospital because of some lower abdominal cramps, and the rupture was discovered at operation.

It is interesting to note that this patient again became pregnant and was delivered by a low flap cesarean section about one year after her discharge from the hospital following the above described rupture. At the time of this third and final cesarean section the abdomen was found to be clean, free of adhesions, the uterus well healed, with no evidence of any thinning or weakening along the line of the previously ruptured cesarean scar. A normal baby was delivered at this time, the operation being done before the onset of labor. No part of the placenta from the previous pregnancy was found. The patient was sterilized by the Pomeroy technique.

SUMMARY

Low flap cesarean section does not prevent rupture of the uterine scar in a subsequent pregnancy, but does decrease greatly the probability of that accident occurring. Available statistics indicate that it occurs only 1/16 as frequently as in patients having the classical type of operation. The predisposing causes seem to be, (1) infection following the previous operation, (2) improper suturing of the wound, and (3) insertion of the placenta at the site of the previous low flap cesarean section scar.

A case is reported in which the uterine scar of a previous low flap cesarean section presumably ruptured early in pregnancy as the result of trauma, the product of conception being completely expelled into the abdominal cavity, where it developed four weeks past term as a secondary abdominal pregnancy. Suture of the ruptured uterus at this time resulted in good union, so that a subsequent pregnancy was carried to term. Extensive and careful search of the literature has revealed no similar case.

REFERENCES

- (1) *Krukenberg*: Arch. J. Gynäk., 1886. (2) *Porro*: Milano, frat. Rechiedei, 1873. (3) *Harris*: Am. J. Obst. 11: 620, 1879. (4) *Sänger*: Leipzig, 1882, Der Kaiserschnitt bei Geburtskunde. (5) *Findley, Palmer*: Am. J. Obst. 74: 420, 1916. (6) *Davis, Asa B.*: AM. J. OBST. & GYNEC. 13: 522, 1927. (7) *La Mariana*: Modern Times & Long Island M. J. 61: 307, 1933. (8) *Kerr, McIntyre, and Hendry*: Brit. M. J. 1: 1093, 1924. (9) *Audebert, J. L.*: Gynéc. et obst. 7: 487, 1923. (10) *Holland, E.*: Lancet 2: 591, 1920. (11) *Weber, G. H.*: Illinois M. J. 47: 39, 1925. (12) *Wettenwald, Max*: Zentralbl. f. Gynäk. March 6, 1926; Gynéc. et obst. 13: 131, 1926. (13) *Gellé, P.*: Bull. Soc. d'obst. et de gynéc. 21: 62, 1932. (14) *Cameron, S. J.*: Proc. Roy. Soc. Med. 16: 50, 1923. (15) *Perez, M. L., and Talioferro, F.*: Semana. méd. 1: 1443, 1936. (16) *Waters, E. G.*: Personal Communication, April, 1938.

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DISCUSSION

DR. ALFRED C. BECK.—I have yet to see a rupture of the scar following a low cesarean section in labor, much less in pregnancy. That is a rather remarkable fact when one considers that the low section was originally restricted to those cases in which labor had been rather prolonged, in which many vaginal examinations had been done or in which the membranes had been ruptured for a long time.

When infection was present, no doubt the uterine wound broke down in places and a sinus was formed which drained through the lower angle of the abdominal incision or back through the lower segment and cervix into the vagina. That such a sinus has developed was demonstrated in several cases that I have cared for. In these when the bladder was peeled off at a subsequent section, a small opening was

revealed. In spite of the fact that these openings when present constituted a defect in the lower uterine segment, rupture did not take place in the subsequent pregnancy.

DR. HAROLD C. INGRAHAM.—I would like to ask the doctor what incision was made in these cases, whether transverse or linear.

DR. ELIOT BISHOP.—The only instance I can recall where a presumable rupture of a low flap cesarean scar occurred was one from Dr. Beck's clinic. This patient, in her first labor, had a 9-pound baby which was subjected to craniotomy, and in her second labor she had a 5-pound baby which was delivered by cesarean section, which according to the records reported to us had been of the low flap type.

The patient to whom I have referred was hospitalized only a few days before term. The operation was planned for 8:00 A.M. At about 3:00 A.M. one or two pains occurred and then the patient went into shock. She was sectioned, transfused, and recovered. The baby had been extruded into the abdominal cavity and was dead.

I was very much interested last June while in London, to note how commonly most of the men there used buried silk or linen sutures in their gynecologic cases and apparently in most of the cesarean sections also. Mr. Eardley Holland's well-known investigation of hundreds of ruptures of the scar following cesarean section stimulated Mr. Leslie Williams to search the literature but he found *no* case of rupture of the scar where the uterus had been repaired with nonabsorbable sutures.

DR. E. EVERETT BUNZEL.—We have had in the last year and a half three cases of rupture following the low flap section, at Sloane Hospital. One of these cases was previously done at Sloane, one at Bellevue Hospital, and one in an institution whose name I have forgotten.

Dr. Geppert said that his case was one of ante-partum rupture, and yet he stated that this patient was uncomfortable for several hours prior to the time that the rupture occurred. Possibly those uncomfortable hours were beginning pains of labor. In other words, it may have been not an ante-partum but an intrapartum rupture.

DR. WILLIAM E. STUDDIFORD.—The extension of the rupture into the upper uterus, noted by Dr. Geppert would suggest that at the time of the first cesarean section the incision had not been completely confined to the lower uterine segment. I am certain also that in a case quoted by Dr. Bunzel, the incision partly involved the upper uterine segment. When she was admitted to Bellevue Hospital, she was in the eighth month of pregnancy, and was not in labor. She had a complete separation of the placenta following an automobile accident, and it would have been very unusual for her to have a lower uterine segment sufficiently developed at this time to permit delivery.

About two years ago we had a most illuminating case at Bellevue Hospital which illustrated very well the relative healing qualities of an incision in the upper segment of the uterus and in the lower uterine segment. This patient had been in labor for about ten hours with ruptured membranes, and because labor had come to a standstill it was decided to do a low flap section on her. At the time of operation an incision was made in the lower segment of the uterus, when the patient began to show evidence of shock, and because the operator was hurried, the fetus was delivered as a breech. In doing this he extended the incision up to the top of the fundus of the uterus, so that, in effect, he had two incisions in the same uterus, a low flap incision which he made with a knife, and a classical incision which was caused by extension. The patient ran a febrile course for two or three days, but did not seem to be in particularly bad condition. On the fourth day, however, she suddenly presented all the signs and symptoms of general peritonitis and died about the tenth day after operation. At autopsy it was found that the low flap incision had healed by primary union. The tear which had passed through the contractile part of the uterus was wide open so that there was a large fistula from the uterus into the peritoneal cavity.

It seems fairly easy to explain this. An incision which is made in the lower uterine segment passes through tissue which is relatively quiescent, noncontractile, and even if catgut is weakened by a low-grade infection, it has a very marked

tendency to heal. When we have an incision through the contractile part of the uterus, however, the very contractions, in the face of weakened catgut and of infection tend to break this part of the uterus open.

DR. VINCENT P. MAZZOLA.—About twelve years ago I performed a low double flap cesarean section on a patient with contracted pelvis and membranes ruptured for many hours. On the tenth day postoperative, the patient passed the entire line of sutures per vaginam. Two years later she became pregnant again. An elective low double flap cesarean section was done after a short period of labor. After peeling off the lower flap, examination of the old scar revealed perfect union. This single experience impressed me with the fact that although the entire row of sutures had previously been passed ten days postoperative, the low section scar healed with primary union and hence was less liable to rupture.

DR. WILLIAM H. CARY.—I would like to ask the doctor if he will elucidate what happened to the placenta in this case. I understand it was left attached to the gall bladder and the liver.

DR. GEPFERT (closing).—We made a point of looking up the relative figures on transverse and vertical incisions. The only two things that stand out are that in using the vertical incision there is a little tendency to tear into the muscular part of the uterus during the delivery of the head and shoulders. In doing the transverse incision there is a tendency to profuse bleeding in the lateral extensions. As far as the relative occurrence of rupture goes, there seems to be no difference between the two modifications of the technic.

In answer to Dr. Bunzel, I would say that we have no definite way of knowing just when this woman ruptured her uterus. We believe she ruptured it sometime during the third month, otherwise we would not expect to get a complete transference of the placenta. The placenta was definitely attached to the liver and to the gall bladder and was not free in the abdominal cavity. The edges of the uterine rupture were dry and everted. There was no free blood and very little fluid in the abdominal cavity. On that basis, we presumed that the rupture was a very old one and that the woman had a true secondary transplacental, and abdominal pregnancy. In this case the umbilical cord was brought out through the upper angle of the incision. Drainage persisted for about five weeks.

PUERPERAL STERILIZATION

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DURING the last fifteen months at the Chicago Lying-in Hospital, 50 women have been sterilized by tying off the Fallopian tubes within the first twenty-four hours after delivery. The average number of hours elapsing between the delivery and the operation was 11.5; the shortest time was 1.5 and the longest 23.5 hours.

Skajaa¹ has reported 126 puerperal sterilizations done between the second and twenty-ninth post-partum days. His report covers a five-year period. There is a series of 46 patients who were operated upon between the fifth and twenty-ninth post-partum days. In this group, there were 7 cases of thrombosis and one of embolism, an incidence of over 17 per cent. Thrombosis was especially frequent where the operation was performed five or six days post partum. In a group of 12 cases done on the fifth and sixth post-partum days, there were 4 cases of thrombosis

and 1 of embolism, an incidence of over 41 per cent. He included in his report a series of 80 patients operated upon between the second and fourth days post partum. In this group, there was only one case of thrombosis, an incidence of 1.25 per cent. He enumerates the following probable etiologic factors for thrombosis: (1) less satisfactory general condition of the patient, (2) the use of ether instead of local anesthesia, (3) complicated labor with artificial delivery, (4) post-partum hemorrhage with insertion of hand in the uterus, and (5) demonstrable infection previous to operation.

The morbidity and mortality of our 50 cases of puerperal sterilization are compared with those of a series of 465 cesarean sections and sterilizations. There were 399 lower segment, 7 classical cesarean sections with sterilization, and 59 Porro cesarean sections. The standard of febrile morbidity advocated and approved by the American Committee on Maternal Welfare was used in calculating the morbidity. This standard is as follows: any patient with a temperature of 38° C. (100.4° F.) or over, recorded on any two days after the first twenty-four hours post partum, oral temperature readings being made at least 4 times daily, is regarded as febrile. The incidence of febrile morbidity in the 50 cases of puerperal sterilization was 6 (12 per cent). The maximum temperature was 101.5° F. and not one of the febrile cases had a fever which lasted more than two days. The febrile morbidity in the 7 classical cesarean sections was 85.7 per cent; 59.5 per cent of the Porro cesarean sections were febrile, and 40 per cent of those having a lower segment cesarean section had a febrile reaction. The average morbidity for all types of sterilization combined with cesarean section was 43 per cent, in comparison with 12 per cent morbidity in the present series.

The average period of postoperative hospitalization was 11.3 days. The febrile cases were discharged between the ninth and fourteenth postoperative days. In the whole series there were two minor wound infections which healed rapidly. Both of these patients were afebrile. They were discharged on the thirteenth and fourteenth postoperative days, respectively. There were no deaths in the cases of puerperal sterilization, whereas in the cesarean section and sterilization group, there were 4 deaths, an incidence of approximately 1 per cent.

Labor was induced medically in 10 per cent of these patients at or near term. This was done because of some maternal complications which rendered the continuation of the pregnancy undesirable. One of these patients had a febrile morbidity.

The average parity of the patients was 4.6. The average age of these women was 29.5 years; the youngest was 20 years old, the oldest 42. The former patient was a cardiac with mitral insufficiency, and she had three other living children. A local anesthesia was used exclusively in these 50 cases. The usual preoperative medication consisted of $\frac{1}{4}$ gr. of morphine and $\frac{1}{150}$ gr. of scopolamine given $1\frac{1}{4}$ hours preoperatively and $\frac{1}{6}$ gr. of morphine and $\frac{1}{200}$ gr. of scopolamine given one-half hour preoperatively. The dosage was varied somewhat depending on the size of the patient, those of lighter weight being given a smaller dose than those of heavier weight.

However, in cases of cesarean section with sterilization, preoperative medication with barbiturates and morphine is not used frequently in conjunction with local anesthesia because of the excitation of the patient and the possible effects of these drugs upon the fetus.

The technique of the operation is relatively simple: local infiltration anesthesia with 0.5 per cent novocaine solution is used in the abdominal wall and within the peritoneal cavity. A small median incision is made immediately below the umbilicus. The round ligament is grasped with the fingers, exposing the uterine horn together with the tube. The Fallopian tube is gently grasped with Allis forceps and 1 to 2 c.c. of a 0.5 per cent novocaine solution is injected between the leaves of the mesosalpinx. The tube is kinked by pulling it forward with the Allis clamp. The tube is then clamped on both sides of the Allis forceps and then crushed about 1 cm. on either side of the forceps with a hemorrhoidectomy clamp. Black silk and catgut have both been used by passing the suture through the mesosalpinx, and then tying it tightly over the crushed areas of the tube. The opposite horn of the uterus is exposed and the tube is treated in the same manner.

Puerperal sterilization has many advantages. We have tried this procedure to determine its efficacy and safety as compared with other means of sterilization. The carrying out of this procedure within twenty-four hours after delivery avoids the questionable procedure of cesarean section for sterilization and the necessity of subsequent hospitalization and operation for sterilization. It also avoids the loss of time and the expense of the subsequent hospitalization period. The period of hospitalization subsequent to delivery is not prolonged more than one or two days. In analyzing our cesarean sections, it was found that many of them were done where sterilization was an important consideration and was used as an indication for the procedure. Doubtless, similar conditions exist in other clinics and institutions. Obviously, our series is not large enough to draw any final conclusions relative to the desirability and safety of this operation as compared with other procedures for sterilization. In this group of cases there was no indication for cesarean section other than sterilization.

Most of the women were multiparas and the average duration of the labor was approximately seven and one-half hours. There were only 6 cases where labor was more than ten hours and in 1 the labor was less than one-half hour. These cases were selected with very great care and every effort was made to eliminate those who had a potential genital infection. There were no cases of mechanical induction of labor. All genital manipulations prior to or during labor were considered as hazards and such cases were automatically excluded. Where there was danger of the introduction of infection, either ante partum, intra partum, or post partum, from procedures, such as difficult operative deliveries, manual removal of the placenta, post-partum hemorrhage, etc., puerperal sterilization was not done.

In the whole series of cases the average length of time which elapsed between the rupture of the membranes and the delivery was 5.1 hours, though 3 patients with membranes ruptured for more than forty hours

showed no morbidity. There were 6 deliveries with low forceps, 1 of which was febrile. The other patients delivered naturally.

There is practically nothing in the literature relative to the puerperal sterilization. F. E. Whitacre, formerly of our staff, suggested the procedure of sterilization immediately following delivery. Not being in favor of subjecting recently delivered women to such an operation immediately after the termination of labor, the above procedure was adopted.

The following outline gives the indications for which puerperal sterilizations were done:

	CASES
<i>Cardiac</i> (27)	
Rheumatic heart disease with insufficiency	26
Congenital heart disease	1
<i>Cardiovascular</i> (4)	
Hypertensive heart disease	1
Rheumatic heart disease with pre-eclampsia	1
Chronic glomerulonephritis with cardiac disease	1
Essential hypertension	1
<i>Chronic infectious diseases</i> (6)	
Pulmonary tuberculosis	5
Chronic bronchitis with marked arthritis	1
<i>Constitutional diseases</i> (3)	
Diabetes	1
Thyrotoxicosis	1
Anemia of pregnancy	1
(with previous post-partum hemorrhage)	
<i>Neurologic diseases</i> (7)	
Spastic paraplegia with rheumatic heart disease	1
Epilepsy	4
Mixed psychoneurosis	1
Paralysis of lower extremities	1
<i>Vascular diseases</i> (1)	
Marked vulvar varicosities	1
<i>Cardiovascular renal disease</i> (2)	
Chronic nephritis	2
Total	50

It is to be emphasized that in our series of cases there has been neither thrombosis nor embolism.

Recently, E. F. Daily analyzed 1,000 cesarean sections of all types in the Department of Obstetrics and Gynecology at the Chicago Lying-in Hospital. This series was divided chronologically into two groups of 500 each. There were 182 cesarean sections and sterilizations in the first 500 cases as compared with 217 in the second 500 cases. The number and percentage of the cases in which the indication for sterilization was a decisive factor showed an increase of 15 per cent. The major indications of this group were chronic cardiac and other organic diseases. If one considers cardiac disease alone, there was an increase of 97 per cent in the second series of cases over the first series, in which the operation was done largely because of the indications for sterilization. In the chronic nephritic group there was an increase of 143 per cent in the second series as compared with the first. There was an increase of 2.7 per cent of

febrile morbidity in the second series of cesarean sections with sterilizations over the analogous cases in the first group.

Of the 406 cesarean sections and sterilizations, 287 were done by the Madlener technique and 119 by resection of the tubes. In comparing the first 500 with the second 500 cesarean sections, there was a decrease of tubal resection from 74 to 45 cases, a drop of 40 per cent. The use of the Madlener technique increased 56 per cent. In our series only one case was done by means of tubal resection. The others were done by the Madlener technique.

We are inclined to believe that this is both a desirable and safe procedure in women who are neither actually nor potentially infected by genital manipulations prior to or during labor. Unless other indications actually exist for performing cesarean sections, we are of the opinion that it is better to follow natural delivery with this method of puerperal sterilization than to resort to cesarean section.

It is in patients who have a natural delivery, particularly in multiparas with rather short labors, that puerperal sterilization within twenty-four hours is indicated.

CONCLUSIONS

We have made a preliminary report of 50 cases of puerperal sterilizations performed within twenty-four hours after delivery. The morbidity and mortality of these patients are compared with those of patients who were subjected to cesarean section with sterilization. Preoperative basal anesthesia with local infiltration anesthesia was used exclusively in carrying out the technique of this operation. We are eliminating cesarean sections for sterilization. The cases were carefully selected and potential infection was regarded as a contraindication to the performance of puerperal sterilization. This operation may be considered as a desirable substitute for late sterilization. In case no contraindications exist, it is performed within twenty-four hours subsequent to delivery. At the present time we are of the opinion that puerperal sterilization, subsequent to the first twenty-four hours after delivery, is not a desirable procedure and that the necessity of sterilization should not lead us to perform a cesarean section in the absence of other indications.

REFERENCE

- (1) *Skajaa, K.*: Acta obst. et gynec. 12: 114, 1932.

Krusen, Randall, and Stuhler: Fever Therapy Plus Additional Local Heating in the Treatment of Gonorrhea, Am. J. Syph., Gonorr. & Ven. Dis. 22: 185, 1938.

The authors found that in women in whom a pelvic inflammatory disease proved refractory to fever therapy alone, the addition of local pelvic heating in conjunction with fever therapy produced most encouraging results.

With proper preparation and follow-up treatment, single ten-hour sessions of fever therapy at 41.5° C. (106.7° F.) will produce negative cultures in a high percentage of cases of gonorrhea.

C. O. MALAND

GRANULOMA VENEREUM OF CERVIX UTERI

A STATISTICAL STUDY

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THE cervix uteri is now recognized as a site for the lesion of granuloma venereum (inguinale), either with or without ulcerations elsewhere.¹ This exuberant granulomatous ulceration of the cervix simulates carcinoma so closely that the diagnosis is usually made only after histologic study of a biopsy. The frequency of this specific condition has never been determined, yet granulomas of the cervix have been described since 1928. Gardner² suggested that such granulomas may possibly be related to granuloma inguinale (venereum). In 1934 McGee³ reported eight cases of cervical granuloma, in none of which was he able to demonstrate Donovan bodies. He classified these lesions as a nonspecific granuloma but observed that five of his patients responded favorably to treatment with tartar emetic. It is interesting to note that his patients were negroes, from 19 to 60 years of age, and in each a tentative clinical diagnosis of carcinoma was made.

Granuloma venereum (inguinale) of the cervix was not established as a definite entity until 1937¹ and it was then observed that the Donovan bodies had an affinity for silver. This observation followed a previous description⁴ of a specific histology for granuloma venereum and a pathognomonic cell was discerned. In regard to granuloma venereum of the cervix, questions now arise as to its numerical, racial and age incidence; symptomatology; its association with ulcerations elsewhere. We have reviewed all sections of cervixes which have been examined in our laboratory for the past ten years. The criteria for the diagnosis were based upon the observations made in a former article.⁴ In all cases that were accepted as positive, the pathognomonic cell was observed. This is a large cell which contains intracytoplasmic cysts; and the round or rodlike Donovan bodies are grouped peripherally within the cysts.

From our previous studies on venereal diseases we have recognized histologic characteristics which frequently enable us to diagnose, in addition to granuloma venereum, lymphogranuloma venereum and chaneroid.⁵ In lymphogranuloma venereum there is pronounced peritubular infiltration with plasma cells and lymphocytes, accompanied by fibroblastic activity, dilated lymphatics, and in some cases with giant cells of the foreign body type. Occasionally foci of suppuration are noted, similar to that type of reaction seen in buboes, necrotic centers surrounded by macrophages. The chaneroid is characterized by superficial necrosis infiltrated with polymorphonuclear leucocytes. In the surrounding area plasma cells, lymphocytes, and endothelial leucocytes are also present. There is an acute peri- and endovasculitis with pronounced swelling of the endothelium, frequently blocking the lumen of the capil-

laries and leading to necrosis. The vascular changes are characteristic and responsible for the superficial necrosis and unhealthy granulation.

We were unable to find a single case of granuloma venereum of the cervix in the files prior to 1934. However, since 1934 nine cases were observed. This confirms the impression shared by our colleagues that venereal granuloma is on the increase. The 9 cases were found in the 830 biopsies of the cervix which were performed between Jan. 1, 1934, and March 31, 1938. This is 1.1 per cent of all cervixes that were biopsied. Of these 830 patients, 694 were white and in none was the diagnosis of granuloma venereum made. Of the biopsies from the 136 negro patients, 9 were positive for granuloma venereum, an incidence of 6.6 per cent. If the 69 carcinomas are eliminated from this group, we find that 13.4 per cent of the remaining 67 negro patients who complained of cervical lesions, suffered from granuloma venereum.

No especial age incidence could be established from this small group. Like McGee's patients with nonspecific granuloma, ours varied in age from 18 to 62 years. It does occur (Table I) most commonly in the periods of sexual activity, thus lending support to the assumption that this is a venereal disease.

TABLE I. SYMPTOMATOLOGY

AGE	ULCERATION	TESTS	PREG-NANCIES	DIS-CHARGE	BLEED-ING	ABD. PAIN	LOSS OF WEIGHT	BACK-ACHE	DURATION	RED CELLS IN MILLIONS	HG
18*	Vulval	Chanc. + Frei -	Now preg-nant							2.9	56%
20	Vulval	None	0	+		+		+	1½ yr.		50%
22	Vulval	Wass. - Chanc. + Frei +	?	+					1 yr.		
27	None	Wass. - Kahn -	2	+		+			9 mo.	2.5	70%
33*	None	Wass. + Chanc. + Frei +	3	+	+				4 wk.	3.9	70%
39	None	Chanc. + Frei -	9	+		+			2 mo.		
47	None	None	0	+	+				3 mo.		
56	None	Wass. -	3	+	+		+		3 mo.	4.1	74%
62†	Inguinal and vulval	Wass. - Frei - Diabetic	3	+					2 yr.	3.9	70%

*Reported previously by Pund and Greenblatt.

†Reported previously by Dr. M. E. Ross.

SYMPTOMATOLOGY

The duration of complaints, from which the patients sought relief, varied from two months to two years, with an average of eight months. Eight patients complained of vaginal discharge and in 3 of these the discharge was blood stained.

Three suffered some pain in the lower abdomen, 1 complained of backache, and 1 had lost weight. The 6 hospitalized patients exhibited a varying degree of anemia. It is interesting to note that these symptoms suggest carcinoma, and in 5 this was the presumptive clinical diagnosis. A presumptive diagnosis of granuloma venereum was made in four instances. These 4 patients were seen in the past two years while a group study of the venereal diseases was being conducted at the University of Georgia School of Medicine.

Five of the patients had borne children, and 1 of the remaining 4 was pregnant. Four patients were tested with Frei and chaneroid bacillary antigens. Two of these had positive chaneroid tests and in one of these the histologic lesion suggested chaneroid as well as venereal granuloma. The other 2 patients reacted positively both to the chaneroid and Frei antigens, and in both of these the histology suggested chaneroid. One patient, a diabetic, was tested with Frei antigen and did not react. She, however, had a history of a previous bubo. Four patients were not tested for venereal lymphogranuloma or chaneroid. The histologic lesion of one suggested lymphogranuloma venereum and the ulcerations were accompanied by elephantiasis of vulva. One had a history of gonorrheal infection; one had previously been operated upon for pelvic inflammatory disease; and in the section from the fourth patient, the histology suggested granuloma venereum complicated with chaneroid.

In our experience, multiple infections⁵ are so common that we believe that granuloma venereum usually occurs superimposed upon other conditions. The histories, physical findings, and histology suggest that this disease in most of these patients was superimposed upon gonorrheal cervicitis, chaneroid infection or lesions of lymphogranuloma. The lesion was limited to the cervix or cervix and vagina in 5 cases, and in 3 to the cervix alone. In the other 4 cases, ulcerations were also present on the vulva, and in only 1 was an inguinal ulceration present.

SUMMARY

From a study of 830 biopsies of diseased cervixes of the uterus, the lesion was due to granuloma venereum in 9 cases, an incidence of 1.1 per cent.

In biopsies from negro patients the incidence was 6.6 per cent.

In biopsies from negro patients without carcinoma of the cervix, the incidence was 13.4 per cent.

We have never observed granuloma venereum of the cervix in a biopsy from a white patient.

Nine cases of granuloma venereum of the cervix have been found since 1934. No cases were observed six years prior to 1934.

The cervix uteri may be the primary site of granuloma venereum, and is often a complication of other venereal diseases.

The symptoms suggest carcinoma.

REFERENCES

- (1) Pund, Edgar R., and Greenblatt, R. B.: J. A. M. A. 108: 1401, 1937.
- (2) Gardner, G. H.: Gynecology, by Howard A. Kelly and collaborators, New York, 1928, D. Appleton & Co.
- (3) McGee, W. B.: AM. J. OBST. & GYNEC. 28: 244, 1934.
- (4) Pund, Edgar R., and Greenblatt, R. B.: Arch. Path. 23: 224, 1937.
- (5) Pund, Edgar R., Greenblatt, R. B., and Huie, Georgia B.: Am. J. Syph., Gonorr., & Ven. Dis. 22: 495, 1938.

THE BLOOD CHEMISTRY IN ERYTHROBLASTOSIS FETALIS

REPORT OF THREE CASES WITH ABNORMAL FINDINGS

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ERYTHROBLASTOSIS fetalis is still an obscure enough disease to merit reporting any new findings which might throw light on its pathogenesis, symptomatology, or treatment. With this in mind I wish to report three proved cases with distinctly unusual blood chemistry findings.

In a brief review of the literature including the classical reports of the disease,¹⁻³ I found no reference to unusual findings in the blood urea, blood uric acid, and blood chloride values. Moreover, the conclusions as to the serum protein values are not in agreement. The clinical, hematologic, and pathologic pictures are fairly uniform in all cases, but except for the bilirubin determinations the other chemical determinations seem to have been overlooked. The reason for this is probably the technical difficulty in obtaining sufficient blood from newborns for complete analysis. In addition possibly usual changes were not suspected or present.

REPORT OF CASES

The following three cases were all seen at the Sinai Hospital, Baltimore, Maryland:

CASE 1.—Baby E. The sixth gestational product of Mrs. E., aged 31, whose previous pregnancies terminated as follows: (1) Normal full-term parturition at Sinai Hospital. Child alive and well aged 11 years. (2) Full-term parturition, child developed jaundice and died at Johns Hopkins Hospital at the age of one month. No autopsy record was obtained; the diagnosis was icterus gravis. This was in 1926 before erythroblastosis was recognized as a clinical entity. (3) Full-term stillborn at Sinai Hospital; cause of death not determined. (4) Premature infant that lived three days. (5) Full-term stillborn, intranatal death. This labor was induced by 25 gr. of quinine. This was thought to be a possible cause for intrauterine death.

During the pregnancy now under consideration a thorough study for the cause of the fetal deaths was made. Diabetes mellitus was excluded by a normal blood sugar and a normal glucose tolerance test as well as by the absence of glycosuria. Syphilis was eliminated by a negative Wassermann and Kahn reaction. However, on the advice of the syphilologist one course of the antisyphilitic therapy was given in the early part of pregnancy. The patient exhibited no evidence of either early or late toxemia. In view of the patient's story that towards the end of each preceding pregnancy, she had noticed that in the last month the fetal movements became less pronounced and finally ceased, it was decided to admit her for induction of labor, without quinine, three weeks before term. Labor was induced and the delivery was normal.

At birth the child cried immediately and respiration was established spontaneously. The vernix was scant and white and the placenta was normal in size and consistency. The characteristic thick yellow vernix caseosa was not present. The delivery was at night and in the artificial light no jaundice was noted. Eight hours after delivery the child developed jaundice. Hematologic study revealed an erythroblastic anemia with characteristic findings. The hemoglobin was 90 per cent, red blood count

3,350,000 per c.mm., with a color index of 1.3. The acetic acid residue showed 80,000 nucleated cells of which 45,600 were nucleated red cells and 34,000 were leucocytes. The Schilling differential showed 15 per cent early white cells, mostly myelocytes and metamyelocytes, 45 per cent polymorphonuclear neutrophils, 30 per cent lymphocytes, 8 per cent monocytes, 2 per cent basophiles. The nucleated red cells were macronormoblasts and normoblasts. The red cells in the smear showed

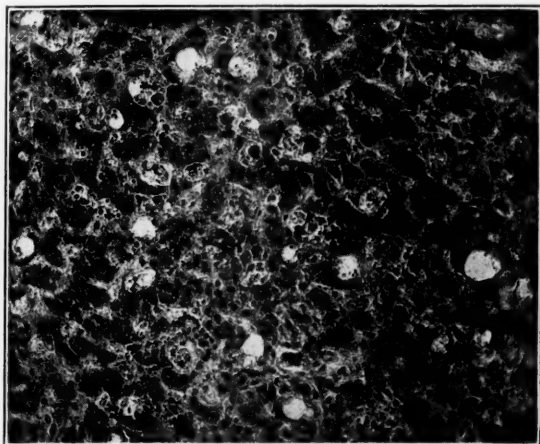


Fig. 1.—Baby E. Erythroblastosis with icterus gravis. Section of the liver showing foci of erythroleucoblastic activity. Deposits of hemosiderin were numerous.

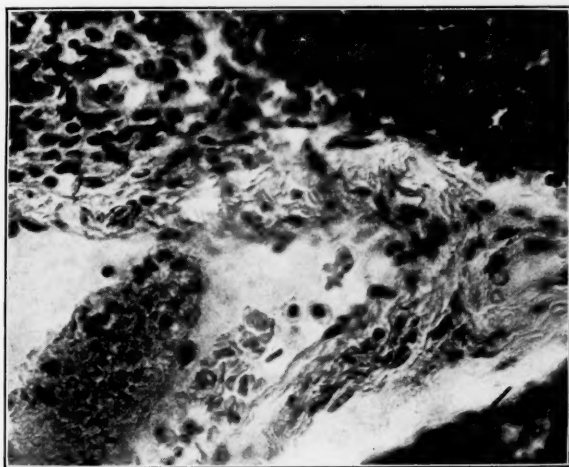


Fig. 2.—Erythroblastosis with icterus gravis. Section of thymus showing typical macronormoblasts growing in an extramedullary focus of blood production.

anisocytosis with predominance of macrocytes. The clotting and the bleeding time were within normal limits. The platelets were moderately reduced. The fragility test was normal. The Wassermann test was negative and the roentgenologic examination of the long bones failed to show syphilis. The icterus index was 100, and the van den Bergh bi-phasic. The gastric contents (vomitus) revealed bilirubin, ruling out biliary obstruction. The urine had a trace of bilirubin and urobilin. The stools were positive for bilirubin and urobilin.

The child had an enlarged spleen and liver and, in a few days, developed rigidity of neck and limbs. During the following eight days the jaundice became more intense, pallor appeared, and the anemia became progressively worse. However, the nucleated red cells gradually became less numerous and by the tenth day were entirely absent. At this time the icterus index was 150 and the urea was 200 mg. per cent.

The child was treated with a concentrated formula, daily clyses of 5 per cent glucose, and repeated blood transfusions, but on the eleventh day developed a temperature of 103° F., with physical signs of pneumonia, and died. A complete autopsy grossly revealed bile stained viscera, a liver of 200 gm. and a spleen of 50 gm. The lungs presented evidence of pneumonia complicated by hemothorax. Microscopic examination of the viscera demonstrated extramedullary foci of active hematopoiesis in the liver, spleen, kidney, pancreas, adrenals, thymus, pituitary, and lymph nodes. These foci on examination presented areas of erythroleucoblastic activity. Hemosiderin deposits were found in the liver and spleen.

This case is noteworthy for the definite familial history and the blood urea of 200 mg. per cent.

CASE 2.—Baby B. First pregnancy. At thirty-six weeks the mother developed hydramnios, edema, and dyspnea. This was so marked that we considered the possibility of interruption. The urine showed a one-plus albumin. The phenolsulphone-

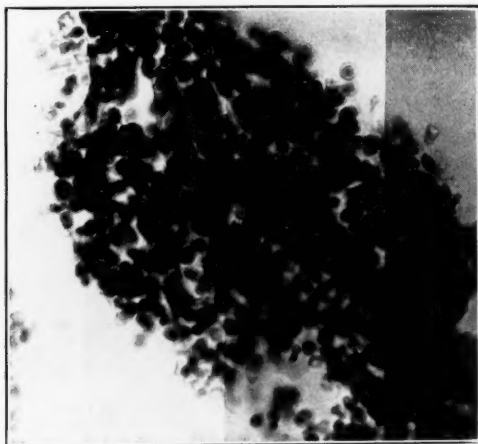


Fig. 3.—Section of the bone marrow showing abnormal number of erythroblasts.

phthalein test showed 65 per cent recovery in two hours. The blood chemistry was essentially normal: Urea 24 mg. per cent, chloride 371 mg. per cent, and total serum protein 7.8 mg. per cent, with an albumin globulin ratio of 2. The uric acid was elevated to 5.3 mg. per cent. The maternal Wassermann reaction was negative. The hydramnios and edema failed to respond to conservative treatment and the pregnancy was interrupted at thirty-six weeks by medical induction followed by artificial puncture of the membranes. Labor was uncomplicated and the second stage was terminated by an episiotomy and low forceps delivery of a live female child which weighed 6 pounds 12 ounces. The general condition of the child was poor. The temperature was 96° F., the heart action slow and irregular, cry weak, and respirations slow and shallow. It was quite difficult to resuscitate and intratracheal aspiration, water baths and artificial respiration, followed by intratracheal insufflation with a resuscitator were necessary before the infant was breathing regularly. The infant kept expectorating frothy sputum.

Physically the infant presented generalized anasarca involving especially the face, hands, feet, and chest. The skin was pale and cyanotic. The heart was not enlarged and there were no murmurs. The chest presented diffuse moist râles. The abdomen presented physical signs of ascites. The liver, spleen, and kidneys were not palpable.

There was marked vulval edema and the extremities had pitting edema. The placenta was large and friable but the vernix was normal in color and consistency. A hematologic study revealed a macrocytic anemia. The hemoglobin was 75 per cent. The red blood count 2,960,000. The color index was therefore 1.25. The total acetic acid resistant count was 7,600 with 34 per cent of them nucleated red cells. The Schilling differential count showed 47 per cent polymorphonuclears, 44 per cent lymphocytes, 1 per cent monocytes, 6 per cent myelocytes, and 2 per cent juveniles. The urine was scant, with one-plus albumin and 5-6-plus cells per high power field. The blood chemistry was again abnormal. The urea was 40 mg. per cent and the uric acid 8.5 mg. per cent. The chlorides were 144 mg. per cent. The serum protein was 7.4 per cent with an A/G ratio of 4.3. The blood Wassermann reaction was negative as were the x-rays of the long bones.

The infant was placed in a heated crib with continuous pure oxygen supply interrupted by frequent carbon dioxide inhalations. Whole blood was given intramuscularly but the infant became gradually worse and died within twelve hours. A few hours before death, 0.5 c.c. of mereupurin was given intramuscularly but failed to exert any manifest action before death. The autopsy grossly revealed marked anasarca with particular edema of the face and the extremities, ascites, and hydrothorax. The viscera were pale and edematous but aside from that were grossly normal. The liver and spleen were small, weighing 120 and 5 gm., respectively. The kidneys were normal in size and shape. Microscopically, extramedullary blood production was evident in numerous organs. There were foci of active hematopoiesis of the erythro-leucoblastic variety in the liver, spleen, thymus, pancreas, adrenals, lymph nodes, and bone marrow.

This case of hydrops is noteworthy chiefly because of the potential toxemic status of the mother combined with the unusual blood chemistry of the offspring.

CASE 3.—Baby F. First pregnancy. Delivered normally at term, weighed 7 pounds 6½ ounces, and was born jaundiced. The amniotic fluid was bile stained, and the vernix was thick and yellow but the placenta was normal. Physical examination revealed splenomegaly in addition to severe icterus. Within the twenty-four hours after birth the child developed dyspnea, cyanosis, and refused nourishment. A few hours later the child had marked hematemesis and moderate vaginal bleeding.

The blood count revealed a severe anemia with the color index slightly above one, the hemoglobin being 25 per cent and the red blood count 1,200,000 per c.mm. Smear and white count were not obtained. Blood urea was 60 mg. per cent. No other laboratory tests were done as the child died within twenty-eight hours after delivery. The only treatment given was whole blood intramuscularly and calcium lactate by mouth.

The post-mortem examination grossly showed a large spleen and hemorrhages into the kidney, uterus, serosa, and pericardium. Microscopically, the organs showed typical areas of extramedullary erythro-leucoblastic activity.

This case is noteworthy only because of the typical clinical and pathologic findings, a very severe congenital anemia associated with icterus and the elevated blood urea.

COMMENT

In all three cases of erythroblastosis presented there were abnormal blood chemistry findings varying from slight nitrogen retention to uremia. The nonprotein nitrogen and blood urea were elevated in all three cases, and the blood uric acid was elevated in the first two. This is in favor of renal insufficiency as a significant factor in the fatal cases, at least, since all these three infants died. The six kidneys examined pathologically from these three cases failed to exhibit any organic changes of nephritis or nephrosis. It may be that in newborns, renal insufficiency may result from functional changes incident to a severe anemia, or secondary to an intercurrent infection or preceding death from erythroblastosis.

As regards the pathogenesis of erythroblastosis a suggestion as to the underlying difference in the clinical pictures of icterus gravis, hydrops fetalis, and congenital anemia is found in contrasting the clinical pathologic findings in these cases. In hydrops, although the nucleated blood cells in the peripheral blood were only moderately increased, the foci in the viscera were exceedingly plentiful, thus favoring the view that in hydrops fetalis the pathogenesis lies either in overgrowth of immature forms, or a failure of maturation of erythrocytes. However in icterus gravis in which the nucleated red cell count is higher, and the foci in the viscera less plentiful the etiology lies in the delivery of these immature forms to the circulation with resulting increase in destruction. Hellman and Hertig,⁴ in a study of 13 autopsies on infants who died of hydrops fetalis and 6 on infants who died of icterus gravis, also found more extramedullary erythropoiesis in the former group.

The reason for the spasticity in nuclear icterus has never been fully explained even though pigmentation of the central nervous system has been observed. In Case 1, the infant developed spasticity and rigidity of the neck and limbs associated with azotemia. This uremia associated with acidosis may be responsible for the rigidity of the neck and limbs. This type of spasticity is very often seen in so-called nuclear icterus, the outstanding feature of which is the pigmentation of the cerebral nervous system, particularly the large ganglia. It is suggested that the azotemia associated with icterus gravis may be responsible for the central nervous system symptoms frequently found in nuclear icterus.

In explanation of the edema, in erythroblastosis with hydrops fetalis some authorities have stressed the albuminuria, decrease in total serum protein, and reversal of the A/G ratio as the cause. In Case 2 the albuminuria was slight, the serum protein normal, and the A/G ratio accentuated strongly suggesting another cause for the edema. The total urinary output was diminished and this oliguria combined with azotemia speaks for renal insufficiency as the cause of the edema. The low blood chloride is best explained by the loss of chloride with the edema, anasarea, and effusion fluids. The low chloride value is seen also in cases of nephritis with edema and in cases of nephrosis.

CONCLUSIONS

1. Azotemia is a frequent complication in severe cases of erythroblastosis of all types, and when present makes the prognosis much worse.
2. This azotemia may be the responsible factor in the central nervous system symptoms in nuclear icterus.
3. Renal insufficiency, per se, and not albuminuria and decrease in serum protein, is the more probable cause of universal edema of the newborn.
4. In the absence of signs of acute nephritis, mercurial diuretics along with blood transfusions and lyophile (concentrated human serum) seem to be indicated in treating the edema.

SUMMARY

Three fatal cases of erythroblastosis fetalis are presented, one with icterus gravis, one with hydrops fetalis, and one with congenital anemia,

all of which showed abnormal blood chemistry: azotemia, which is therefore regarded as an unfavorable prognostic sign.

The author wishes to thank Dr. Daniel Sondheimer, resident pathologist at Sinai Hospital, Baltimore, Md., for the pathologic examinations and for helpful suggestions in the preparation of this paper.

REFERENCES

- (1) Clifford, S. H., and Hertig, A. T.: *New England J. M.* 207: 105, 1932. (2) Blackfan, Kenneth D., Diamond, L. K., and Baty, J. M.: *J. Pediat.* 1: 269, 1932. (3) Astrachan, Morris: *Am. J. Dis. Child.* 53: 137, 1927. (4) Hellman, Louis M., and Hertig, Arthur T.: *AM. J. OBST. & GYNEC.* 36: 137, 1938.

PRECOCIOUS PUBERTY DUE TO AN OVARIAN CYST IN A FIVE-YEAR-OLD GIRL

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N. A., aged five years (Hospital Number E 6088), was first seen July 13, 1935, with the history of considerable breast development during the previous two months. On the day before consultation, the child while sitting on the toilet, announced, "Cherry juice is running down my legs." On inspection definite blood mixed with mucus apparently coming from the vagina, could be seen on the inner surface of each thigh. Subsequently a study of the visual fields and a roentgenogram of the sella turcica were done and revealed no abnormalities.

The breasts were definitely enlarged (Fig. 1, A) and the parenchyma was nodular and shotty. There was bloody mucus with a typical menstrual odor surrounding the vulva, and the external genitalia, although small and in proportion to the child's size, presented such adult characteristics as brownish pigmentation and well-developed and sharply-defined labia minora. In addition, the vaginal mucosa was not only unlike that of a prepuberal child but also was thrown into definite folds resembling rugae. There was no well-defined axillary or pubic hair although on close inspection a few scattered hairs could be seen on the mons veneris. Rectobimanual examination was done under anesthesia the following morning. The uterus was enlarged almost to the size of that of an adult virgin. There was a cystic, symmetric mass, the size of a golf ball, in the left adnexal region, but nothing was palpable on the right side. Biopsy of the vaginal epithelium taken at this time showed (Fig. 2) hyperplastic mucosa with a stratified, considerably thickened, squamous epithelium slightly cornified in some areas, and with a papillated basal layer.

Exploratory laparotomy was performed on July 16, 1935. The right ovary was small, the size of a navy bean, and its surface was smooth, presenting no follicles. It was the typical ovary of a child. The left ovary was replaced by a smooth, glistening cyst 4 to 5 cm. in diameter (Fig. 3). Both tubes were extremely long and tortuous and with the uterus were approximately of adult size. In fact, with the exception of the right ovary, all of the intra-abdominal genitalia presented adult characteristics. Careful palpation of each kidney and suprarenal area revealed nothing unusual. Left salpingo-oophorectomy with cornual excision and appendectomy were performed.

The report of Dr. H. P. Smith is as follows: "The left ovarian mass measures two and a half by four centimeters in diameter. The surface is smooth and beneath it can be seen several cysts three millimeters in diameter. On section several larger cysts are found. They are lined by a smooth yellow membrane. Microscopically the lining of the cysts is composed of polyhedral cells several cells in thickness. Some resemble granulosa cells; others have vacuolated cytoplasm, like that of lutein cells. The stroma between the cysts is of the normal mature type.

There is no evidence of malignancy. Ordinarily, cysts of this type are not regarded as being neoplastic. Disturbances in other glands of internal secretion, e.g., the hypophysis, might produce this effect. However, if this were true, it is difficult to understand why cysts did not form in the other ovary. Diagnosis: Granulosa cell cysts of left ovary." (Fig. 4.)

The convalescence was uneventful and to date (three years later) the child has been entirely well without recurrence and has been developing in an entirely normal fashion (Fig. 1, *B* and *C*). She has returned to the prepuberal condition of a normal female child with one exception; the breasts, although smaller, softer and less nodular, remain slightly larger than is to be expected of a girl eight years of age.

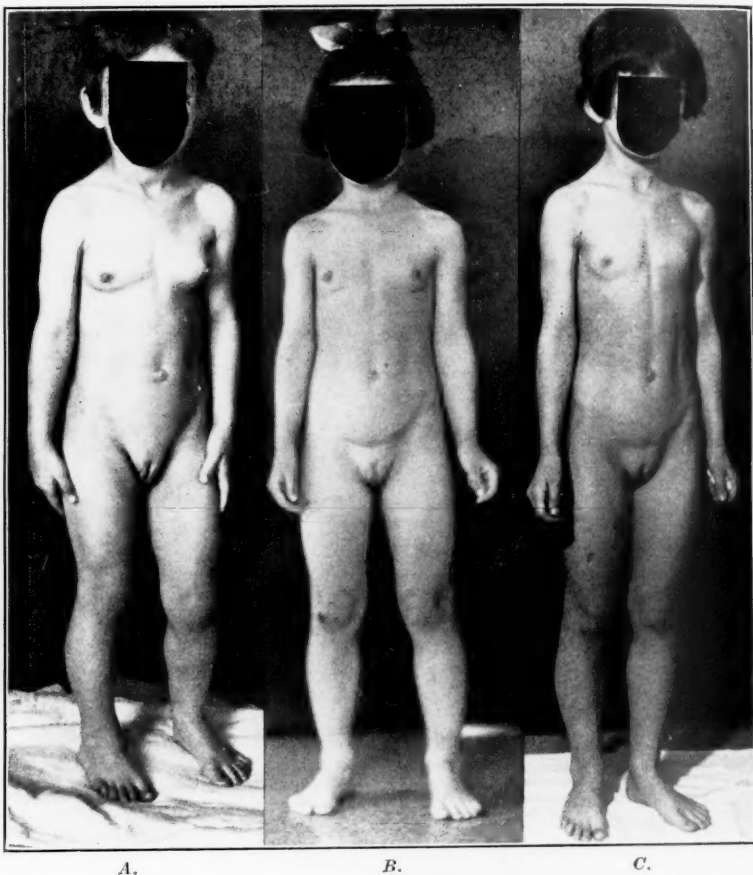


Fig. 1.—*A*, Preoperative condition, aged 5 years; *B*, nine months postoperative; *C*, two and one-half years postoperative.

HORMONAL STUDIES*

The hormone content of the cystic fluid, of pre- and postoperative urine specimens, and of a urine specimen taken in January, 1938, was investigated. There were 1,000 rat units per liter of the estrogenic hormone in the preoperative urine specimen. Approximately 35 c.c. of fluid were aspirated from the extirpated cyst and contained the estrogenic hormone in a concentration of 20,000 rat units per liter.

*These were done in the Department of Zoology through the courtesy of Professor Emil Witschi.

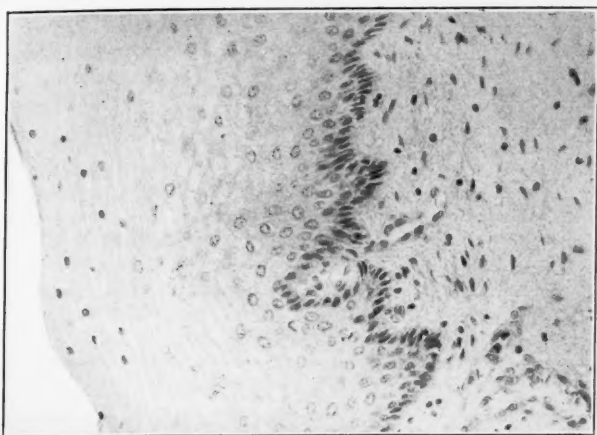


Fig. 2.—Biopsy of vaginal epithelium showing thickening, cornification, and papillated basal layer.

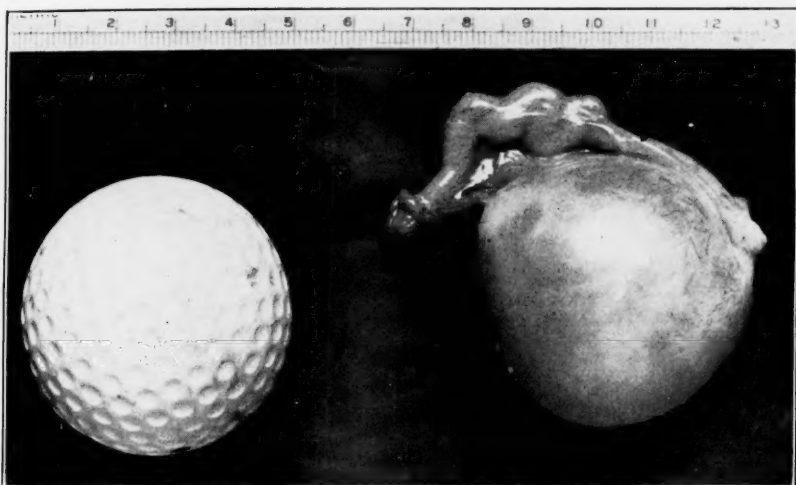


Fig. 3.—Mass removed at operation, contrasted with a golf ball. Note the adult characteristics of the Fallopian tube.

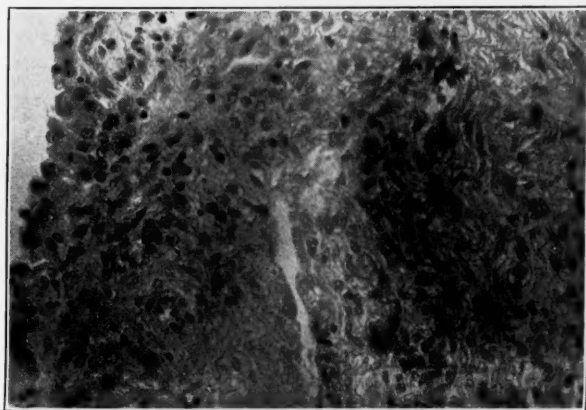


Fig. 4.—Section of cyst wall.

Neither the urine specimen obtained during the first postoperative week, nor that obtained in January, 1938, two and one-half years after operation, gave any reaction in test rats.

DISCUSSION

Three views concerning the nature of the tumor can be entertained. It may have been: (1) a follicle cyst developing as the result of some hormonal stimulus originating elsewhere in the body; (2) a follicle cyst arising independently of any extragenital influence; (3) a primary neoplasm arising independently in the ovary.

If the tumor was a follicle cyst developing as the result of some hormonal stimulus originating elsewhere in the body, perhaps in the hypophysis or adrenal, it is difficult to credit such a stimulus with a selective action affecting only one ovary. Moreover, no tumor of hypophysis or adrenal was discovered although such a possibility was considered. Were such a tumor present, and undiscovered despite the diagnostic efforts to find it, one would have expected the child to have developed similar cysts in the remaining ovary in the three years which have elapsed since operation, and for these cysts to have given evidence of their presence by further precocious sexual development. Instead the patient has had a completely normal physical development and the breasts have regressed noticeably in size. (Fig. 1, B and C).

Follicle cysts apparently may arise independently of any extragenital influence, and Adair and Watts¹ have shown that the fluid may contain relatively high concentrations of the estrogenic hormone. However, such cystic development in a five-year-old girl is rare and difficult to understand.

The view that the cyst was a primary neoplasm is open to the objection that it contained no cells suggesting such origin. As Doctor Smith points out, "... ordinarily cysts of this type are not regarded as being neoplastic."

At any rate, there seems to be little doubt that this tumor was not malignant. Whatever its origin and its nature these basic facts remain: (1) there was sufficient estrogenic hormone in a unilateral ovarian cyst to account for precocious puberty in a five-year-old girl; (2) the premature sexual development ceased abruptly with the removal of the cyst; (3) the child has remained well and normal over a three-year period since extirpation of the cyst.

REFERENCE

- (1) *Adair, Fred L., and Watts, Ruth M.*: AM. J. OBST. & GYN. 34: 799, 1937.

Jacoby, Wishengrad, and Koopman: An Evaluation of the Complement Fixation Test for Gonorrhea, Am. J. Syph., Gonorr. & Ven. 22: 32, 1938.

The authors state that a total of 760 patients were examined by complement fixation for gonorrhea by two different techniques with agreement in 81 per cent of the examinations. This group consisted of cases under treatment and cases for diagnosis.

In the first group, 80 per cent had positive tests. In the second group 38.5 per cent had positive tests.

In the first group the greatest number of positive tests were present in patients having gonorrhea with complications, and those in whom the disease had been present for a period of from one to six months.

A large percentage of positive tests were found in patients with acute infections and in those in whom the infection had been present less than three weeks.

In the group of patients for diagnosis, from 13.4 to 15.5 per cent showed non-specific positive reactions.

The complement fixation test for gonorrhea has but a limited usefulness and is not reliable for diagnostic purposes. With further refinement and standardization of the technique, the test may eventually become more specific.

C. O. MALAND

RUPTURE OF URINARY BLADDER COMPLICATING EARLY PREGNANCY

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IT HAS long been known that a gradually increasing obstruction of the urethra may be caused by a retroverted pregnant uterus. Such an obstruction is relieved either by replacement of the uterus spontaneously or by manipulative means, or goes on to complete obstruction with the retention of large amounts of urine in the bladder as the growing uterus becomes incarcerated in the pelvic cavity. The following case is reported because, in addition to the retention of urine, the unusual complication of rupture of the bladder was present.

Mrs. E. C., aged 38, gravida ii, para i. Wassermann negative. Date of last menstrual period, Dec. 19, 1937. Expected date of confinement, Sept. 26, 1938.

The patient was admitted to the hospital at 10:30 P.M. on March 12, 1938, complaining of severe suprapubic pain of about one hour's duration, which began following an attempt at intercourse. Actual penetration did not occur, the weight of her husband causing a sudden onset of pain in the region of the bladder. She stated that she had experienced difficulty in voiding for several weeks prior to the present illness, at times passing very small amounts of urine, at other times large amounts and, occasionally, not being able to pass any. During this time she had a sense of discomfort in the region of her bladder, apparently not severe enough for her to seek medical advice. For several days prior to the onset of the present illness, the patient stated that she had been able to void very small quantities of urine at longer intervals. She noticed that her abdomen was gradually increasing in size.

The patient was in a state of moderate shock, her color somewhat cyanotic and her respirations increased. Her abdomen was the size of a seven to eight months' pregnancy. There was marked tenderness over the entire abdomen, more marked over the suprapubic region in the midline. Involuntary spasm and rigidity were present over the entire abdomen, more marked over the lower half. Shifting dullness was elicited. The blood pressure was 108/75, the red blood count was 3.4 million, the white blood count was 27,750 and the hemoglobin was 88 per cent. On catheterization six ounces of bloody urine were obtained.

There was no evidence of trauma around the urethra or in the vagina. An old laceration of the perineum with extensive rectocele was present. The anterior vaginal wall gave excellent support. The cervix was firm, closed, slightly hypertrophied and pushed forward and up behind the symphysis. The uterus was completely retroverted, enlarged to the size of a three and a half months' pregnancy and firm in consistency. It was not movable.

A diagnosis was made of intraperitoneal rupture of the urinary bladder. The patient was given an infusion of 2,000 c.c. of saline and prepared for an immediate laparotomy. During this time signs of shock had progressed; the patient was more cyanotic, respirations more rapid, pulse 144, weak and of poor quality. Another attempt was made to catheterize the patient before operation, and 800 c.c. of bloody urine were obtained.

Under cyclopropane anesthesia, the abdomen was opened through a suprapubic midline incision. On opening the peritoneum there was a gush of bloody fluid of uriferous odor. It was possible to measure 4,500 c.c. of this fluid, and the estimated total fluid in the peritoneal cavity was over 6,000 c.c. The bladder was collapsed, the wall being markedly thickened. In the center of the superior portion of the posterior wall, there was an irregular rupture measuring approximately 4 cm. in diameter, the edges of which bled slightly. The opening in the bladder was repaired by three inverting rows of sutures, using number 0 chromic catgut. This was ac-

complicated with some difficulty because of the friability of the bladder musculature. Inspection of the pelvis revealed an enlarged uterus, the size of a three to four months' pregnancy, completely retroverted. No other abnormalities were noted. A cigarette drain was placed deep in the pelvis behind the bladder, and a rubber dam drain was inserted in the space of Retzius. The abdomen was then closed in layers. A retention catheter was inserted in the bladder. Immediately following the operation the patient was given a transfusion of 750 c.c. of whole blood.

The postoperative condition was good. Blood pressure 110/70. The course was quite uneventful. On the first postoperative day there was some cyanosis; respirations were 26 per minute. The urine output was over 1,000 c.c. in the first twenty-four hours and remained satisfactory thereafter. The abdomen remained soft, and at no time was there any distention. The wound healed by primary union. The drain in the space of Retzius was removed on the third postoperative day, and the pelvic drain taken out on the sixth. The indwelling catheter was removed on the eleventh day. Following the removal of the indwelling catheter, the patient was

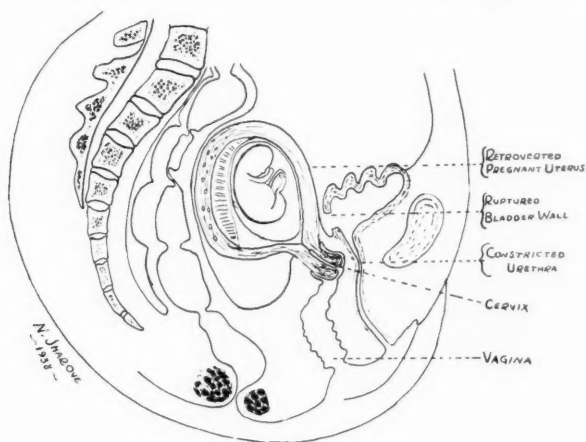


Fig. 1.—The left half of the pelvis with corresponding half sections of the bladder, cervix, uterus and rectum. The pregnant uterus is seen retroverted, and the cervix is shown obstructing the urethra. The approximate site of rupture in the posterior wall of the bladder is shown.

catheterized after each voiding and 600 to 800 c.c. of urine obtained each time. An attempt was made to increase the contractility of the bladder by administration of an ampoule of pituitrin every eight hours for four doses and an ampoule of pitocin every eight hours for four more doses without any improvement.

A neurologic examination of the patient showed no evidence of a spinal cord lesion.

On the first postoperative day, the patient aborted spontaneously a three and a half months' fetus, and three days later expelled a foul smelling placenta and membranes intact.

The patient was cystoscoped on the nineteenth postoperative day, the bladder appearing well healed. No other lesions were noted on this examination. The amount of residual urine gradually decreased to 300 or 400 c.c. The patient was not able to empty her bladder completely, even when up and about.

On the twenty-seventh day, she developed an acute follicular tonsillitis and was transferred to the Ear, Nose and Throat Service. She made an uneventful recovery and was discharged on April 12, the thirtieth postoperative day.

May 3, 1938. Since her discharge from the hospital, the patient has been feeling well. She voided three or four times daily, in fairly large amounts, and usually once during the night. She complained of no urinary symptoms. The abdominal wound was found to be well healed. On pelvic examination a moderately large rectocele was found to be present. The anterior vaginal wall showed fairly good support.

The cervix was hypertrophied, smooth, and pointed up and behind the symphysis. The uterus was normal in size, partly retroverted, and movable. After voiding, 400 c.c. of urine were obtained on catheterization.

June 27, 1938. The patient stated that she felt well and had no complaints. No urinary symptoms were present. She was voiding normal quantities of urine three to four times daily, and occasionally during the night. The pelvic examination was the same as on previous examination. The cervix was behind the symphysis, the uterus partly retroverted. She voided 500 c.c., and upon being catheterized immediately after voiding, 270 c.c. of urine were obtained. The uterus was replaced and a No. 4 pessary inserted.

July 1, 1938. The patient had no complaints. On examination, with the pessary in place, the cervix was found to be directed posteriorly and the uterus was in fairly good position although not completely anterior. She voided 580 c.c. and a residual of 160 c.c. was obtained on catheterization, immediately after voiding. At this visit the uterus was brought up in better position and a No. 5 pessary inserted.

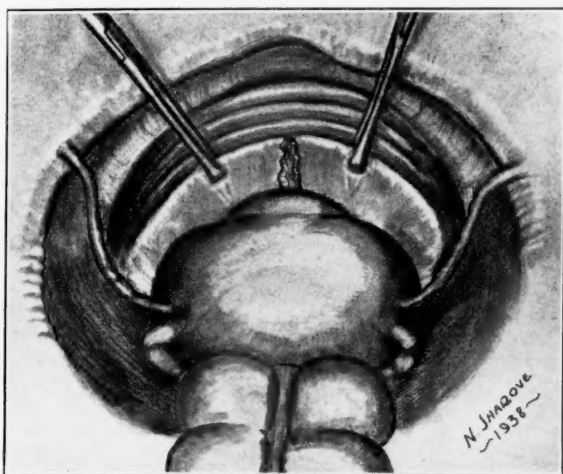


Fig. 2.—Direct view looking into the pelvis at operation, showing retroverted incarcerated uterus. The bladder is held up to show rupture in the posterior wall.

July 8, 1938. The patient had no complaints. She stated she voided more often in smaller amounts, four to five times daily and once during the night. On examination the uterus was in excellent position with the cervix away from the urethra. On this visit, the patient voided 150 c.c. and 55 c.c. were obtained on catheterization immediately after voiding. The pessary was removed and not reinserted, although the uterus and the cervix resumed their original position.

Summary.—A case is described in which rupture of the bladder occurred following an attempt at intercourse. The patient's history suggests a gradually increasing urethral obstruction due to a retroverted three and a half months' pregnant uterus which had become incarcerated in the pelvis. This had eventually resulted in the retention of large amounts of urine in the bladder. Because of distention of the bladder and consequent thinning of its wall, rupture occurred with relatively slight external trauma. Of special interest is the effect of this process on the bladder mechanism. Due, probably, to prolonged distention, the normal tone of the bladder was lost, resulting in the presence of large amounts of residual urine, not affected by treatment. Gradually the bladder regained tone, resulting in a progressively decreasing residual urine. It is not believed that the correction of the uterine displacement influenced this process.

ESTROGENIC HORMONE IN THE URINE AND TUMOR OF A PATIENT WITH A GRANULOSA CELL TUMOR OF THE OVARY*

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THE estrogenic hormone determinations reported here were obtained from the study of a 19-year-old, single, Jewish female.† Her chief complaint was constant vaginal bleeding for more than a year. A firm left-sided freely movable adnexal tumor the size of an orange could be palpated pelvically. Complete twenty-four-hour urine specimens were obtained twice before operation, daily for ten days following operation, and at weekly intervals for five weeks following her discharge from the hospital. In addition to the urine, specimens of blood, tumor tissue, and ovarian cyst fluid were obtained for study on the day of operation. The vitamin C content of the tumor has been determined.‡

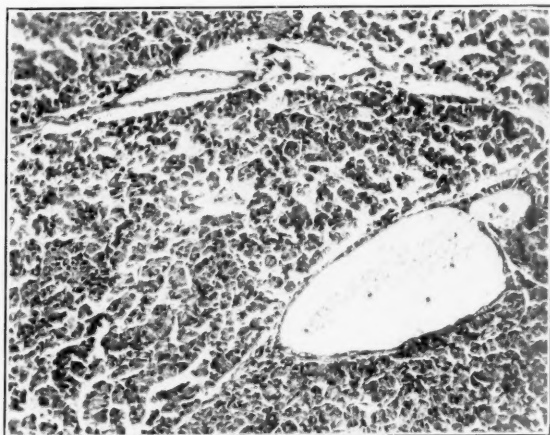


Fig. 1.—Granulosa cell tumor of the ovary. Photomicrograph of solid cellular portion of tumor used for bio-assay. ($\times 100$.)

Gonadotropic Hormone.—A quantity of each twenty-four-hour specimen was concentrated after the benzoic acid precipitation procedure of Katzman and Doisy.² None of the specimens of urine, obtained before or after the operation, was found to contain any active principle that showed its effect by activation of the ovaries of immature female mice. The blood, tumor tissue, and ovarian cyst fluid were not tested for gonadotropic hormone. The Friedman pregnancy test was negative.

Estrogenic Hormone.—It seems advisable to restate that in the assay of unknown estrogenic hormones by a biologic method, the result must be in terms of an estrogenic equivalent, inasmuch as the biologic method cannot be specific for one type of estrogen unless the chemical identity of that hormone is known.‡ All values for estrogenic hormone computed for this patient are equivalent to the estrogenic activity of crystalline estrone.

*This study made possible by a grant from the Christine Breon Fund for Medical Research in the University of California.

†Miss R. F., a private patient of Dr. D. A. Susnow. The pathological and clinical aspects of the case are to be reported by Dr. G. Y. Rusk and Dr. R. Rypins.

‡The ability of very small amounts of urine, obtained from this patient before operation, to produce premature vaginal opening and estrus in immature female mice, in the absence of ovarian stimulation, indicates that possibly the chief estrogen excreted was estriol.

Each extract for assay was prepared so as to obtain total estrogenic hormone content by acid hydrolysis of the urine at pH 1. The details of the method used have been outlined elsewhere.³ The possible importance of determining the "free" and "combined" estrogenic hormone proportions was not fully realized at the time extracts were prepared; but a parallel assay procedure carried out on one specimen preoperatively, using whole urine, indicates that the urinary estrin was excreted almost entirely in its "free" state. The test animals used throughout were controlled according to a plan already described.⁴

The estrin content of the blood serum and ovarian cyst fluid was apparently much less than anticipated and consequently was not demonstrated in the amounts of these fluids tested. The estrin content of the tumor was obtained by finding the smallest amount of fresh tumor tissue which, implanted into the peritoneal cavity of

TABLE I. ESTROGENIC HORMONE EXCRETED BY PATIENT BEFORE AND AFTER OPERATION

DATE	URINE SPECIMEN	ASSAY (ESTRONE EQUIVALENT)
10/ 7/35	Preop. 16 weeks	40.0 gamma/24 hours
10/24/35	Preop. 13½ weeks	66.6 gamma/24 hours
1/27/36	Day of operation	86.6 gamma/24 hours
1/28/36	Postop. 1 day	10.0 gamma/24 hours
1/29/36	(Incomplete spec.)	
1/30/36	Postop. 3 days	20.0 gamma/24 hours
1/31/36	Postop. 4 days	8.0 gamma/24 hours
2/ 1/36	Postop. 5 days	6.6 gamma/24 hours
2/ 2/36	(Incomplete spec.)	
2/ 3/36	Postop. 7 days	0.0 gamma/24 hours
2/ 4/36	Postop. 8 days	2.5 gamma/24 hours
2/ 5/36	(Incomplete spec.)	
2/ 6/36	(Incomplete spec.)	
2/ 7/36	Postop. 11 days	4.6 gamma/24 hours
2/20/36	Postop. 3 weeks	11.0 gamma/24 hours
2/27/36	Postop. 4 weeks	0.0 gamma/24 hours
3/11/36	Postop. 6 weeks	0.0 gamma/24 hours
3/18/36	Postop. 7 weeks	13.0 gamma/24 hours
3/25/36	Postop. 8 weeks	4.0 gamma/24 hours
1/27/36	Blood serum	less than 50.0 gamma/liter
	Ovarian cyst fluid	less than 50.0 gamma/liter
	Tumor tissue (desiccated)	11,700.0 gamma/kilogram

TABLE II. QUANTITATIVE ASSAY OF ESTROGENIC HORMONE IN RECORDED CASES OF GRANULOSA CELL TUMOR

AUTHOR	URINE ESTRIN	TISSUE ESTRIN	
		FRESH	DESICCATED
1930 Schuschania ⁵	65 M.U./liter	47 M.U./kg.	
1933 Dworzak ⁶	50 M.U./liter (postop.)		
1935 Bland ⁷	300 M.U./liter		
1935 Geist ⁸		1,000 M.U./kg.	
1935 Geist (Thecoma) ⁹		1,500 M.U./kg.	
1935 Szathmary ¹⁰	360 M.U./liter (postop.)		
1935 Thornton ¹¹	7½ M.U./liter (postop.)		
1936 Gospe ¹²		3,200 M.U./kg.	36,000 M.U./ kg.
1937 Studdiford ¹³	8 R.U./liter (postop.)		
1937 Anderson ¹⁴	17,390 M.U./liter	5,000 M.U./kg.	
1937 Meigs ¹⁵		530 M.U./kg.	
1938 Palmer (this case)	866 I.U./liter (Calculated as estrone)	20,000 I.U./kg. (Calculated as estrone)	117,000 I.U./ kg.

a controlled test mouse, would produce complete vaginal cornification in that animal. The value for desiccated tissue was calculated from that for fresh tissue.

The values for tissue estrin in this case, although higher than others taken from the literature, is conservative, as all such values must be. As yet it has not been possible to prepare a medium containing a known amount of crystalline estrone, for purposes of abdominal tissue implant procedures, that would be similar in every respect to the hormone in tissue cells elaborating that hormone. In a separate experiment an attempt was made to simulate slow continued peritoneal absorption of estrogenic hormone as might occur from a mass of fresh tissue cells, by injecting known amounts of estrone in olive oil solution intraperitoneally into 100 newly castrated mice. This experiment was temporarily abandoned when it was found that not one of the 100 mice developed full vaginal cornification after the intraperitoneal administration of ten times the cornifying subcutaneous dose of the same oily solution.

DISCUSSION

The amount of estrogenic hormone excreted daily by this patient before operation, while approximately 4 to 5 times the average daily excretion by a normal non-pregnant woman, is about equal to the amount excreted daily by a woman six to eight weeks pregnant. A normal woman may excrete more estrogenic hormone in a single twenty-four-hour period during the peak of hormone excretion, i.e., the midintermenstruum than was excreted daily by this patient with the granulosa cell tumor. However, the point of difference is that this patient was bleeding while excreting the hormone. When a normal woman menstruates, her estrogenic hormone excretion is at its lowest. Usually the amount is not demonstrable.

If a reason needs to be given for a tumor so rich in estrogenic hormone content being associated with only moderately increased excretion of hormone, it may be conjectured that the continuous vaginal bleeding which this patient endured possibly accounted for the greatest loss of estrogenic hormone from her body. Reference to this possible means of excretion associated with fall in kidney excretion of hormone has been made previously.^{3, 16} It is interesting to note also that the only case reported in Table II associated with a tremendous hormone excretion was one of granulosa cell tumor in a child of four who had had no vaginal bleeding. Anderson's patient¹⁴ continued to excrete an excessive amount of estrogen two days after operation, and it was not until some time after the first vaginal bleeding occurring on the third postoperative day, that his patient was excreting normal amounts of hormone. On the other hand, in my report the excretion of estrogenic hormone was normal beginning the first postoperative day and thereafter.

SUMMARY

Estrogenic hormone determinations on the tumor and urine of a patient with a granulosa cell tumor of the ovary are reported. Values for the hormone are calculated as estrone. The content of the tumor was found to be 11,700.0 gamma (11.7 mg.) per kilogram desiccated tumor tissue associated with a maximum urinary excretion of 86.6 gamma per twenty-four hours while the patient was bleeding. Beginning the first day after operation the urinary excretion of estrogenic hormone fell to normal. Comparable values from other cases recorded in the literature are tabulated.

REFERENCES

- (1) Biskind, G. R., and Glick, D.: *Science* **84**: 186, 1936. (2) Katzman, P. A., and Doisy, E. A.: *J. Biol. Chem.* **106**: 125, 1934. (3) Palmer, A.: *Proc. Soc. Exper. Biol. & Med.* **37**: 273, 1937. (4) Palmer, A.: *Proc. Soc. Exper. Biol. & Med.* **36**: 123, 1937. (5) Schuschania, P.: *Zentralbl. f. Gynäk.* **54**: 1924, 1930. (6) Dworzak, H., and Podleschka, K.: *Arch. f. Gynäk.* **154**: 441, 1933. (7) Bland, P. B., and Goldstein, L.: *Surg. Gynec. Obst.* **61**: 250, 1935. (8) Geist, S. H.: *AM. J. OBST. & GYNEC.* **30**: 650, 1935. (9) Geist, S. H., and Spielman, F.: *J. A. M. A.* **104**: 2173, 1935. (10) Szathmary, Z.: *Zentralbl. f. Gynäk.* **59**: 2477, 1935. (11) Thornton, H. C.: *Am. J. Cancer* **23**: 522, 1935. (12) Gospe, S. M.: *AM. J. OBST. & GYNEC.* **32**: 495, 1936. (13) Studdiford, W. E.: *Ibid.* **33**: 495, 1937. (14) Anderson, M. X., and Sheldon, E. A.: *Ibid.* **34**: 119, 1937. (15) Meigs, J. V., and Parsons, L.: *New England J. Med.* **216**: 681, 1937. (16) Palmer, A.: *AM. J. OBST. & GYNEC.* **36**: 1005, 1938.

A NEW, NONIRRITATING OPAQUE MEDIUM FOR UTEROSALPINGOGRAPHY

II. ELIMINATION OF ACACIA

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Obstetrics and Gynecology, St. Margaret Memorial Hospital)*

THE use of iodized oils in the x-ray visualization of the uterus and Fallopian tubes is occasionally followed by troublesome reactions. Following its injection, acute "chemical" salpingitis, parametric masses, and occasional allergic reactions have been reported. It has recently been shown by our group^{1, 2} that a solution of mono-iodomethane sulphonate of sodium (skioldan) with acacia is a nonirritating medium for uterosalpingography. Skioldan is not irritating to the uterus and tubes. It is rapidly eliminated from the body through the urine and does not liberate free or inorganic iodine.

These studies did not show, however, the effect of the acacia used as a vehicle nor whether the acacia was eliminated. That a knowledge of the effect and fate of acacia is important is pointed out in the literature by several investigators³⁻⁵ who have shown that acacia when injected in large doses intravenously causes damage to the liver. Others⁶ express the clinical view, however, that, "long continued presence of acacia within the body without apparent harmful effects demonstrates anew its innocuous character in man." We wished to be certain, in addition, that the acacia would not become encysted in the peritoneal cavity, as is so often the case with iodized oil injected for uterosalpingography.

To complete the study of the effect of, and the fate of, skioldan-acacia, a series of experiments was devised to study the action of the acacia upon the uterus, tubes, and peritoneum, if any, and to determine its fate upon injection into the female internal genitalia and the peritoneum.¹

SUMMARY OF EXPERIMENTS

Our experiments with acacia fall into three parts; first, a determination of the local or general effect of the injection of acacia into the genitalia and peritoneum of female rabbits, second, a study of the blood and urine thereafter for acacia, and third, chemical and microscopic studies of the livers of rabbits so injected.

1. Local and General Effects

Three rabbits were injected with varying amounts of acacia in different ways. Rabbit 101 received 2 c.c. of 20 per cent acacia in the uterus and tubes following the technique used in our preceding experiments.² There was no immediate reaction of any kind. After thirty-two days this rabbit was killed and the peritoneum and internal genitalia carefully examined. There was no evidence of the acacia in the peritoneum or genitalia, nor was there any evidence of inflammation or irritation. The liver was examined and found grossly to be normal. Rabbit 102 received 5 c.c. of

20 per cent acacia directly into the peritoneum. There was no immediate reaction and after twenty-five days this rabbit was killed. The gross examination of peritoneum and liver did not show any evidence of irritative effect. Rabbit 103 received 6.6 c.c. of 30 per cent acacia directly into the peritoneum and was killed seven days afterward. In this instance the fluid in the peritoneum contained less than 0.1 mg. of acacia per c.c. with no evidence of irritation, encysting of this substance in the peritoneum, or damage to the liver.

2. Chemical Tests for Acacia in Blood and Urine

There is no specific test for acacia. For studies of acacia in urine Sumner's method⁷ is not effective since acacia does not reduce Sumner's reagent. Normal urine contains materials that produce furfural upon treatment with acid so that a test by the method of Youngberg⁸ must be a differential one. Bial's orcinol-hydrochloric acid reaction for pentose in urine is perhaps the best indication of the presence of acacia in urine.

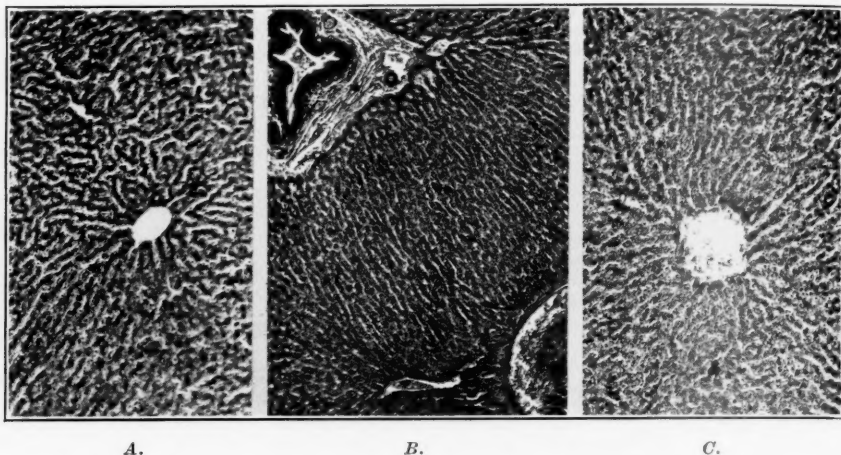


Fig. 1.—A, Rabbit 101 liver thirty-two days after injection of 0.4 gm. of acacia; B, Rabbit 102 liver twenty-five days after injection of 1.0 gm. of acacia; C, Rabbit 103 liver seven days after injection of 2.0 gm. of acacia.

It was found (see Table I) that minute amounts of acacia could be detected in the urine at intervals of from 6 to 108 hours after injection. It was concluded that if acacia is excreted in the urine it must be in only small amounts and perhaps over a very long period of time as was found by Andersch and Gibson.³

For studies of acacia in the blood the oxidimetric method of Keith, Power and Wakefield^{6, 9} was employed, using 95 per cent ethyl alcohol as the precipitating agent. In the first two rabbits we were disappointed not to find the suspected large amounts of acacia in the blood but upon reading the work of Putnam¹⁰ we realized that we were not sampling the blood early enough to pick up the higher levels of the acacia (see Table I). Rabbit 103 showed that the level of acacia reached a maximum at about six hours after injection and rapidly fell to approximately normal in less than seventy-two hours.

3. Chemical and Microscopic Studies of Livers

Several investigators³⁻⁵ have pointed out that the liver is damaged following intravenous use of relatively large amounts of acacia. We felt that we must know if acacia injected into the female internal genitals and peritoneum in the recommended dosage would have a like effect. Rabbits were injected with amounts corresponding to 4 to 20 times the amounts usually used in the human being for uterosalpingography. These rabbits were killed at thirty-two, twenty-five, and

TABLE I. DETERMINATION OF ACACIA IN BLOOD AND URINE

RABBIT	ACACIA INJECTED	URINE		BLOOD	
		TIME AFTER INJECTION	ACACIA BIAL'S TEST	TIME AFTER INJECTION	ACACIA IN BLOOD SERUM
101	0.4 gm.	12 hr.	None	36 hr.	208.0 mg./100 c.c.
		36 hr.	Trace		
		60 hr.	None		
		84 hr.	Trace		
		108 hr.	Trace		
102	1.0 gm.	12 hr.	Trace	48 hr.	13.1 mg./100 c.c. 18.0 mg./100 c.c.
		36 hr.	None		
		42 hr.	None		
		62 hr.	Trace		
		96 hr.	Trace		
103	2.0 gm.	6 hr.	None	3 hr. 6 hr. 24 hr. 72 hr.	30.3 mg./100 c.c. 316.0 mg./100 c.c. 476.0 mg./100 c.c. 312.0 mg./100 c.c. 4.0 mg./100 c.c.
		24 hr.	None		
		72 hr.	Trace		

TABLE II. DETERMINATION OF ACACIA IN LIVER

RABBIT NO.	ACACIA INJECTED	TIME AFTER INJECTION	ACACIA IN LIVER	MICROSCOPIC SECTION LIVER
101	0.4 gm.	32 days	29.9 mg./gm.	Normal
102	1.9 gm.	25 days	23.5 mg./gm.	Normal
103	2.0 gm.	7 days	25.4 mg./gm.	Normal

seven days after injection of acacia. In Rabbit 101 the injection was made into the uterus and tubes while in the remaining two rabbits the acacia was placed directly into the peritoneum. The livers were examined in situ in the gross and were found to present a normal appearance as to shape, size, margins, and surfaces. They were immediately removed from the body and a portion placed in Zenker's fixative for microscopic study and a second portion taken for quantitative estimation of the amount of acacia therein. For this analysis the method of Youngberg⁸ as used by Andersch and Gibson³ was employed. The amount of furfural producing material, calculated as acacia, in all three livers was just above that given by Andersch and Gibson³ as normal (Table II).

The microscopic study of these livers did not show the destruction and swelling of liver parenchyma as found by others following intravenous injection of larger amounts of acacia,³⁻⁵ and it was felt that all sections represent essentially normal histology.

SUMMARY

1. Experimental data indicate that acacia injected in the amounts used in uterosalpingography does not irritate the internal genitalia or peritoneum in rabbits.

2. Acacia does not remain in the peritoneum but is rapidly taken up and appears in the blood stream within three hours following its injection. The maximum level of acacia in the blood is reached within six hours, and it has almost disappeared from the blood in seventy-two hours.

3. We could not prove that acacia is excreted in the urine. It has been shown by Andersch and Gibson that in bile fistula dogs, acacia appears within six hours in the bile, and it is most likely that the bile is the means by which it leaves the body.

4. Microscopic studies of the livers up to thirty-two days after injection of more than ten times the amount of acacia used in human uterosalpingography did not show liver damage.

5. The amount of furfural producing material, calculated as acacia, in the liver was just above that said to be normal.

CONCLUSION

Our previous findings show that skiodan produces satisfactory x-ray shadows, and further is nonirritating to the tissues and is rapidly eliminated from the body. Our present findings show that acacia is nonirritating, is not retained in the peritoneum and does not cause liver damage. We conclude that skiodan-acacia in uterosalpingography is harmless in the amounts used and is, therefore, to be preferred to the older opaque media (iodized oils).

The materials for this investigation were generously furnished by the Winthrop Chemical Co., New York.

REFERENCES

- (1) Titus, P., Tafel, R. E., McClellan, R. H., and Messer, F. C.: *AM. J. OBST. & GYNEC.* 33: 164, 1937. (2) *Idem*: *Ibid.* 36: 889, 1938. (3) Andersch, M., and Gibson, R. B.: *J. Pharmacol. & Exper. Therap.* 52: 390, 1934. (4) Heckel, G. P., Erickson, C. C., Yuile, C. L., and Knutti, R. E.: *J. Exper. Med.* 67: 345, 1938. (5) Hall, W. K.: *Proc. Soc. Exper. Biol. & Med.* 38: 46, 1938. (6) Keith, N. M., Power, M. H., and Wakefield, E. G.: *Proc. Staff Meet., Mayo Clinic* 10: 38, 1935. (7) Sumner, J. B.: *J. Biol. Chem.* 65: 319, 1925. (8) Youngberg, G. E.: *J. Biol. Chem.* 73: 599, 1927. (9) Power, M. H., and Wakefield, E. G.: *J. Biol. Chem.* 123: 665, 1938. (10) Putnam, T. J.: *Am. J. Physiol.* 63: 548, 1923.

RELAXATION OF THE PELVIC LIGAMENTS IN PREGNANT MONKEYS

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PROFOUND changes occur in the pubic and sacroiliac joints in many of the lower mammals during the course of gestation. The hormonal control of the tissue metamorphoses involved has been fairly well worked out.¹ An examination of modern textbooks of obstetrics^{2,3} as well as the current literature on the subject indicates that pelvic relaxation in women is generally recognized. Most of the clinical literature concerns cases of pathologic exaggeration of the process which may lead to separation of the pubic bones and consequent distressing symptoms. The pregnancy changes in the ligaments as a normal and physiologic process is also stressed or taken for granted. Thus Kehrer³ states that the motility of the pelvic bones, by loosening of the joints, has not only a pathologic significance but above all a physiologic one; for it makes possible an increase in the diameter of the birth canal. DeLee² says that "in the human there is no doubt but that the joints soften, thicken and thus enlarge the cavity of the pelvis. The bones become more movable on each other. . . ."

The relaxation of the pelvic ligaments has been noted in scores of cases in the rhesus monkey (*Macaca mulatta*) and in six specimens

of the bonnet monkey (*M. radiata*) of the Carnegie monkey colony. It is the purpose of the present paper to record these facts.

METHOD OF DIAGNOSIS

The monkey possesses prominent ischial tuberosities over which the skin forms cornified pads, the "sitting pads."⁴ To test the mobility of the pelvic bones, the animal is laid ventral side down across a suitable block so that the tuberosities are turned up. Each of these is grasped by a thumb and traction placed upon them. The amount of spread is measured by means of calipers and the result is recorded in millimeters. The spread of the joints, if considerable, may also be felt readily by pressing a finger into the clefts formed in the symphyseal joint.

In this experiment most of the symphyseal spread is caudal and very little at the cranial margin of the pubis. This is due to the rotation of the innominate and a tilting of the acetabular borders, as one would expect from a study of the parts in a prepared skeleton. The rotation may also be proved in the living animal, placed on its side, with a lever laid across the lateral margin of the innominate bone. On spreading the tuberosities the long free arm of the lever may be seen to dip by reason of a depression of the edge of the rotating innominate. This may also be regarded as evidence of relaxation in the sacroiliac joints.

In pregnant women, Abramson, Roberts and Wilson⁵ could also regularly demonstrate the mobility of the pelvic bones by tactile examination. While an assistant alternately pulls on one leg and pushes on the other the examiner is able to feel, with his finger placed over the symphysis, the movements of the bones with reference to each other.

RESULTS

Nonpregnant Controls.—Some males and many nonpregnant females were tested as controls. For these animals the figures are without exception low, usually 1 or 2 mm. Some females, however, had pelves uniformly more mobile, registering differences of 3 or 4 mm. These were mostly multiparas, though some multiparas had tight joints except in pregnancy. The ligaments of males and castrated females never showed the slightest looseness. In most females the stage of the menstrual cycle made no difference; but a few females gave the impression of slight relaxation (doubling the spread) toward the end of the cycle.

Pregnant Females.—Some typical cases are the following:

Rhesus Monkey No. 51:		
July 11, 1932,	one month before parturition	2.0 mm.
Aug. 1,	11 days before parturition	10.0 mm.
Aug. 12,	parturition	
Aug. 13,	day after parturition	11.0 mm.
Rhesus Monkey No. 2:		
	Eighty-first day of pregnancy	4.0 mm.
	106th day of pregnancy	4.5 mm.
	At parturition 1933	16.0 mm.
Rhesus Monkey No. 173:		
March 1, 1932,	30 days before parturition	10.0 mm.
March 10,	10 days before parturition	12.0 mm.
March 31,	parturition	18.0 mm.
April 3,	4 days post partum	8.0 mm.
April 19,	19 days post partum	3.0 mm.
Rhesus Monkey No. 236:		
Oct. 21, 1933,	7 days before parturition	15.0 mm.
Oct. 28,	parturition	
Nov. 1,	3 days post partum	10.0 mm.
Nov. 10,	13 days post partum	6.0 to 8.0 mm.
Nov. 13,	16 days post partum	6.0 mm.
April, 1934	many tests	3.0 to 4.0 mm.

Bonnet Monkey No. 150:

May 19, 1934,	parturition	
May 21,	2 days post partum	18.0 mm.
May 25,	6 days post partum	16.0 mm.
May 27,	8 days post partum	15.5 mm.
June 22,	one month post partum	2.5 mm.

Monkey No. 36 is of especial interest. On June 30, 1930, she was hypophysectomized, but her subsequent history showed that some pituitary substance was retained. After a long period of amenorrhea she again menstruated and ovulated. On April 18, 1932, she gave birth to a baby. *Six days and 2 days before parturition* the relaxation figures stood at only 5-6, but at the time of parturition the figures were 11-13 and the following day 16 mm. No explanation is offered for this anomalous behavior.

Relaxation is not usually much advanced before the last month of gestation, which in the monkey has a duration of six lunar months (against 10 for the human being). In women relaxation is said to begin in the fourth month, which in absolute time approaches the beginning of relaxation in the monkey. The post-partum reversion to the normal, firm, nonpregnant condition is accomplished within three or four weeks.

Castration during pregnancy in no wise interferes with the loosening of the pelvic ligaments. Nor is a living fetus necessary, for several cases of complete relaxation were noted after the delivery of a dead, even macerated, fetus near term.

The histologic changes in the ligaments are not great, although no exhaustive study of the problem was made. There seems to be no indication of bone growth such as described by Loeschcka⁶ for women, nor is there any bone resorption or transformation of the connective tissue as described for some of the lower mammals. The only change which a section of the symphysis of a pregnant animal showed when compared with the control was a loosening of the connective tissue fibers due apparently to an edema of the tissue. Whether or not this was preceded by formation of new elements by cell multiplication remains an open question.

SUMMARY

Relaxation of the pelvic ligaments is an invariable accompaniment of pregnancy in the rhesus and the bonnet monkeys. The condition becomes manifest in the last of the five and one-half months' gestation period and reverts to the nonpregnant condition of firmness within three or four weeks after delivery. The changes take place despite castration early in pregnancy or death of the fetus. The loosened ligaments are characterized by edema.

REFERENCES

- (1) Allen, Edgar: (New ed. 1938.) *Sex and Endocrine Glands*, Baltimore, 1932, Williams and Wilkins.
- (2) DeLee, Joseph B.: *The Principles and Practice of Obstetrics*, ed. 6, Philadelphia, 1932, W. B. Saunders Co.
- (3) Halban-Seitz' *Biologie und Pathologie des Weibes* 6: article by E. Kehrer.
- (4) Hartman and Straus: *Anatomy of the Rhesus Monkey*, Baltimore, 1932, Williams and Wilkins.
- (5) Abramson, D., Roberts, S. M., and Wilson, P. D.: *Surg. Gynec. Obst.* 58: 595, 1934.
- (6) Loeschcka, H.: *Arch. f. Gynäk.* 96: 525, 1912.

EUTOCIA COMPLICATED BY LYMPHOPATHIA VENEREA, PERIRECTOANAL MASS, AND RECTAL STRICTURE

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RECENTLY Michelson, Crotty and Kasselberg reported the first proved case of lymphopathia venerea with esthiomene associated with pregnancy.¹ Similar cases were reported by Wilson, in 1930; Das, in 1931; and Gaines and McDowell,² in 1936, but these were not confirmed by the Frei test, which is now regarded as determinative in diagnosis of 97 per cent of all cases. Of two cases reported by Dick³ in Germany, one had been diagnosed only on the clinical picture; the other had a positive Frei test. The latter had a rectal stricture but, like the case reported in this paper, Dick's patient did not have esthiomene of labia majora.

We wish to report one additional case in a pregnant colored woman, with rectal stricture and with a perianal mass, 8 by 4 cm., and hypertrophy of both labia majora, who from a positive Frei skin test was diagnosed as having lymphopathia venerea. She gave birth to a normal infant; the latter, like the child in Michelson's report, but unlike the two children reported by Dick, failed to show a positive Frei test.

CASE REPORT

Mrs. L. F., aged 35, grav. vi, para iv, colored, widow, was first admitted to the University of Nebraska dispensary in 1935 with a complaint of a mass about the anus for some ten years. Blood Wassermann was 4-plus and she was put on anti-syphilitic treatment.

In November, 1936, she complained considerably about loose stools and pain in the region of the rectum during defecation and was at that time found to have a positive Frei test. She was treated by antimony and bismuth with some relief of her symptoms. Since that time she has been found to have a positive Frei test on numerous occasions, two different antigens having been used for this purpose.

In October, 1937, she entered the prenatal clinic complaining of an amenorrhea since June, 1937, and was found to be about four months pregnant.

Significant past illness: Gonorrhea and syphilis. In spite of the fact that she has had difficulty with a perirectoanal mass and a stricture of the rectum for some ten years, her obstetric history is significant because of the absence of dystocia caused by rectal stricture.

In 1921 she had an inevitable abortion; in 1923 a living baby girl, short labor; in 1925 a living baby girl, in labor for only one hour; in 1928 a living baby boy, in labor one hour; in 1930 a living baby boy, with a very short labor.

On Jan. 30, 1938, when about seven months pregnant, she was admitted to the University Hospital complaining of severe abdominal pain, numerous loose stools and chills accompanied by a temperature of 102° F. The diarrhea was controlled by paregoric and bismuth and as the patient was not in labor, she was sent home. Following this, she was seen on numerous occasions by the outpatient department for similar attacks of diarrhea until she was readmitted to the hospital March 8, 1938, complaining of chills and fever. Examination revealed the patient at term with a rectal stricture which would not permit of digital examination and a perirectoanal mass about 8 cm. in length by 4 cm. in width, located at the left and somewhat inferior to the anus and a hypertrophy of the labia majora (Fig. 1).

Laboratory Findings.—A catheterized specimen of urine showed 200 W.B.C. per high power field. Hemoglobin 52 per cent, R.B.C. 3,570,000, W.B.C. 10,150, segmented 61 per cent, staff 9 per cent, lymphocytes 26 per cent, monocytes 4 per cent.

Blood Wassermann as well as Kahn tests was negative. The sedimentation rate was 24 mm. in twenty-two minutes.

Blood chemistry: Serum nonprotein nitrogen 23.4 mg. per cent, total serum protein 7.6 per cent, serum albumin 3.8 per cent, serum globulin 3.8 per cent, fibrogen 0.4 per cent. Blood pressure 110/72.

Course in the Hospital.—At time of admission, the patient was apparently suffering from a pyelitis which cleared immediately following delivery. She went into labor on the fourth day following admission and delivered normally, after three and one-half hours of labor, a living female child, weighing 7.5 pounds. A first degree laceration was sustained but of not enough moment to require suturing. A very normal puerperal course followed and the patient was dismissed on the tenth post-partum day. Since then, she has reported to the dispensary and her Wassermann reaction was reported as 1-plus, while both the Kline and Kahn reactions were negative. At present she is again receiving antisyphilitic treatment. The baby's Frei test was negative on the fifth post-partum day and again negative when the child was four months old.

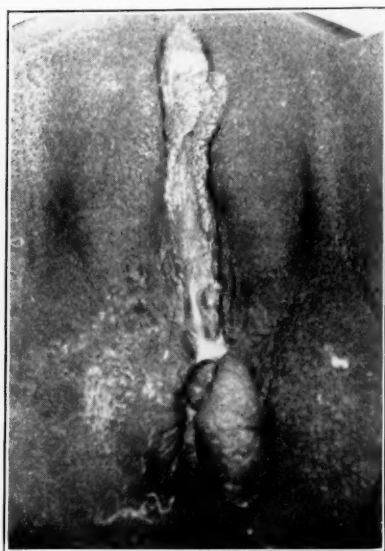


Fig. 1.

DISCUSSION

This case of a colored patient is very similar to the one, also colored, reported by Michelson, Crotty, and Kasselberg with the exception that our case was complicated by perirectoanal mass instead of esthiomene. In our patient's case, the syphilitic background is of comparatively little interest, as in the case reported by Michelson and others. Many investigators report concomitant syphilis in patients with lymphopathia venerea. The clinical and laboratory findings show the patient to have had a chronic condition of lymphopathia venerea during the course of which she successfully gave birth to a normal full term child. Gaines and McDowell,² who report a fatal case of delivery of a woman with a severe rectal stricture due to rupture of the rectum, recommend cesarean section in all such cases. In our patient, no such difficulty with rupture was encountered. Apparently from her former history, since having a perirectoanal mass as complication, she has delivered two other normal living children prior to this time without any harm to either patient or children.

Although changes in the genitalia had not progressed so far that elephantiasis or esthiomene could be diagnosed, yet there was an additional perirectoanal growth

previously described, in addition to hypertrophy of labia majora. The effect of the lymphopathia venerea on fertility is still problematical. Michelson and others, besides reporting the one case, cite only Dick. The latter states, categorically, that females in the late stages of the disease are sterile or unable to find sexual partners; but he gives no proof of sterility nor does he offer explanation for the etiology.

REFERENCES

- (1) Michelson, D., Crotty, J., and Kasselberg, L.: *AM. J. OBST. & GYNEC.* 35: 322, 1938. (2) Gaines, C., and McDowell, J.: *J. A. M. A.* 107: 964, 1936. (3) Dick, Walter: *Med. Klin.* 32: 319, 1936.

ENDOMETRIOSIS OF THE UMBILICUS

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EXTRAPELVIC location of endometrial tissue is uncommon. The umbilicus is one of the rarer locations of endometriosis. Strongin states that only a total of 68 cases have been reported in the entire world until the end of 1935.

I. L., a 40-year-old white, married female, was seen in the Gynecological Clinic of The Barnard Free Skin and Cancer Hospital on Jan. 24, 1938, complaining of abdominal pain and pain in the umbilicus, before, during, and after each menstrual period. This condition was present since the onset of her menstrual cycle, the sequence of symptoms being the same with each menstrual period. The pain started four to five days before each period, continued throughout the period, and persisted for four to five days after its cessation. The umbilicus became quite tender during this time and assumed a bluish discoloration. There was no evidence of external bleeding. Menses began at the age of eleven and appeared every twenty-eight days, and lasted five days. The patient complained of dysmenorrhea and menorrhagia. She had two pregnancies with two normal, full-term deliveries.

The patient had painful breasts with each menstrual period. Two nodules were found in the right breast, both of which were removed, and on pathologic examination proved to be intracanalicular fibroadenomas.

On examination the cervix appeared normal. The corpus was in second degree retrodisplacement, enlarged, freely movable, tender, moderately softened. (Patient examined during premenstrual phase.) There were no adnexal masses or tenderness. The umbilicus was tender, firm, and showed a faint bluish discoloration. No umbilical mass or hernia was present.

The clinical diagnosis was pelvic endometriosis and endometriosis of the umbilicus.

The patient was operated upon on Jan. 26, 1938. The uterus was found to be enlarged three times normal size and densely adherent to the small intestines. The adhesions were difficult to separate. The right ovary contained a blood-filled cyst about 2 cm. in diameter. The appendix was normal. A supravaginal hysterectomy, bilateral salpingo-oophorectomy, and appendectomy were done. The umbilicus was removed, including its underlying peritoneum.

Pathologic Examination.—The umbilicus was 2 cm. wide, surrounding a nodule 1 cm. in diameter, underlying which was a definite tumor mass 2 cm. in diameter. On cut section this tissue contained a number of cysts filled with clear material. Grossly, there was no apparent involvement of the skin. The peritoneal surface was infiltrated with several nodules of tissue, which were hard and irregular. The peritoneal surface of the mass was deeply umbilicated. There were no adhesions of any abdominal viscera to the umbilicus. The wall of the uterus at the internal os measured 3 cm. in diameter. The endometrium was 4 mm. thick, and glistening. The ovaries and appendix appeared as described above.

Microscopically, the umbilical tissue showed numerous endometrial glands, presenting evidence of secretory activity (Fig. 1). The glands varied in size and shape,



Fig. 1.



Fig. 2.

Fig. 1.—Low power section of the umbilicus, showing endometrial glands surrounded by endometrial stroma. In the lumen there is some secretion from the glands. ($\times 130$.)

Fig. 2.—Section of right ovary showing two glands surrounded by endometrial stroma. In the upper left hand corner of the section can be seen a portion of the epithelium covering the ovary. ($\times 130$.)



Fig. 3.

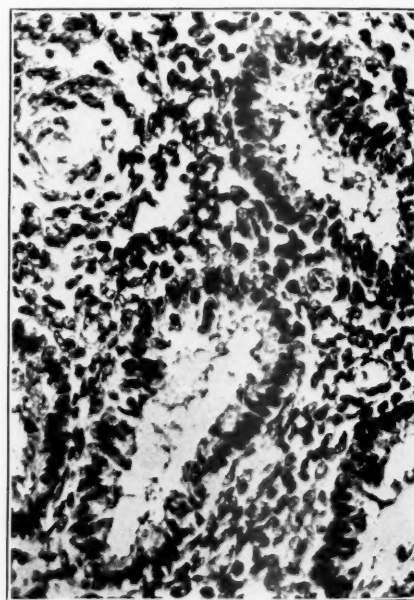


Fig. 4.

Fig. 3.—Section of the endometrium showing glandular hyperplasia with the glands in the premenstrual phase. ($\times 130$.)

Fig. 4.—High power magnification of Fig. 1. The epithelium of the glands is columnar and shows secretory activity. ($\times 540$.)

and were surrounded by a moderate amount of endometrial stroma. There was no microscopic evidence of any infiltration of the skin by the endometrial glands. The section also failed to reveal any involvement of the parietal peritoneum by these glands. The endometrium was hyperplastic (Fig. 3), the state of activity of the glands being similar to that found in the umbilical endometrioma. The wall of the uterus was thickened, due to subinvolution and hypertrophy. The right ovary showed several endometrial glands near its surface (Fig. 2).

INTRALIGAMENTOUS, PAROVARIAN CYST

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ALTHOUGH many instances of very large abdominal tumors have been reported in medical literature, I have not been able to find a record of an intraligamentous, parovarian cyst approaching the size of this one, which is being reported simply as a matter of curiosity.

The patient was a colored woman, thirty-eight years of age, admitted to the Gynecological Service of the Columbia Hospital Feb. 14, 1938. The chief complaint was inconvenience due to her enormously enlarged abdomen. There was no dyspnea while lying quietly in bed, and no edema of lower extremities. The abdominal tumor was noticed first about ten years ago, soon after the delivery of twins, and had gradually increased in size. There had been 11 pregnancies and 11 full-term labors, 4 of these having occurred since the tumor was first detected. Menstruation had always been regular and otherwise normal.

The patient weighed 164 pounds and was 5 feet 1 and $\frac{1}{2}$ inches tall. She was poorly nourished and had extensive oral sepsis. The radial arteries were hard. The blood pressure was 190 over 126. The heart and lungs were displaced upward. The abdomen was greatly distended, having a circumference of 52 inches at the navel and measuring 30 inches from the pubis to the xiphoid. There was an old drainage scar midway between the pubis and umbilicus. Dullness was present throughout and a distinct fluid wave could be elicited over any area. There was no tenderness. The pelvic examination revealed a relaxed pelvic diaphragm with marked cystocele and rectocele. There was a bloody discharge from the cervix, which was drawn high up almost out of reach against the left pelvic wall. The uterus and adnexa could not be palpated. The entire pelvis was filled with a soft, cystic mass which seemed to be pushing the uterus up and to the left.

The hemoglobin was 60 per cent (Dare). The Wassermann and Kahn reactions were negative. A catheterized specimen of urine was negative except for two-plus pus. The kidney function, as determined by the phthalein, blood urea and urea nitrogen tests, was normal.

The diagnosis was large, right ovarian cyst, probably intraligamentous; cystocele; rectocele; oral sepsis, and arteriosclerosis.

Operation was done Feb. 24, 1938. The patient was narcotized with morphine and hyoscine. The skin was infiltrated with novocaine and a small incision made in the midline below the umbilicus. There was extensive thinning of the abdominal wall, which consisted only of skin, fascia and peritoneum. The cyst wall was exposed, a medium sized trocar was inserted into the cyst and 31,000 c.c. of clear, straw-colored fluid drawn off slowly over a period of forty-five minutes. The puncture site was then clamped and tied. The patient was given nitrous oxide and oxygen and the incision extended downward. The tumor wall was adherent by fine adhesions to the anterior parietal wall. With the right horn of the uterus, it was densely adherent to an old scar about midway between the pubis and umbilicus. The cecum and appendix were displaced into the upper left abdomen. The trocar puncture was found to be through the posterior layer of the right broad ligament. The adhesions were released and the anterior layer of the right broad ligament was opened. A line of cleavage was found and the cyst wall, still containing 5,000 c.c.

of fluid, was shelled out from the posterior parietal peritoneum and broad ligament, with practically no bleeding. There was no pedicle and the right ovary was normal. The opening in the broad ligament was sutured and the abdominal wound closed.

The patient's general condition improved during the operation so that, at the end, the original hypertension and rapid pulse rate had dropped to normal. However, when the anesthetic was stopped, signs of shock occurred, but these disappeared as soon as a pillow was strapped tightly over the abdomen.



Fig. 1.

A total of 36,000 c.c., or approximately $9\frac{1}{2}$ gallons, of fluid was obtained from the cyst. The inner surface of the cyst wall was smooth and glistening. The pathologic report was: Massive, serous parovarian cyst.

The patient made an uneventful recovery, was fitted with a surgical corset and dismissed about three weeks after operation. On the day of her dismissal she weighed 74 pounds less than when she was admitted. Six weeks later, she had gained 17 pounds.

A NEW OBSTETRIC PHANTOM

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THE first obstetric phantoms seem to have been constructed and used in the seventeenth century in France. At present there are available fourteen, some of which have definite imperfections. Many other phantoms (about 65) have been mentioned or described but are no longer obtainable. Phantoms like those of Stander, Jacobs or Ayers have seemed the most desirable for demonstrating certain phases of labor and especially forceps deliveries. However, in using some of the others, teachers have been compelled to show the forceps or other maneuvers outside of the phantom rather than in the pelvic cavity, because most of them will not admit of the delivery of a full-term fetus or a doll of corresponding size. Moreover, I am not concerned about reproductions of the abdominal wall or of the uterus, which can be studied safely and to better advantage in living patients. Neither am I much interested in the artificial representation of the vulvar outlet, at best an unsatisfactory makeshift. From any actual delivery one can learn more about this region. The really puzzling thing is what happens within the pelvis itself, and this one can visualize and teach more effectively with one of the three makes mentioned above.

One disadvantage of the metal pelvis has been that in using it, a good forceps may be scratched. To overcome this the Stander pelvis was wrapped with a flannel bandage and a leather doll was used instead of the metal head. Subsequently, the makers substituted for the aluminum head a rubber head and shoulders. Then the writer had the inner surface of the pelvis lined with rubber which was carried over the edges of the bones (Figs. 1 and 2). Serious thought was given to the suggestion to have the pelvic muscles represented in rubber somewhat as they are built up in the University of Oregon obstetric manikin but the idea was abandoned. A number of changes were made by the producing company or initiated by the author. The base was made smaller so that it would fit into a bag. The rod supporting the pelvis was shortened and was moved up to the very edge of the base instead of being three inches back, changes which correspond to bringing the patient's buttocks to the edge of the delivery table, a necessary move in most forceps operations.

From an extension of the spine there was carried out over the pelvic inlet a bar in which holes had been drilled. Into these holes a rod was fastened bent at an angle so that it represented the pelvic curve (Fig. 1). First a flexible copper rod was used until the curve had been determined and then a steel rod was fashioned to that exact pattern. Meanwhile an opening had been made in the top of the rubber head so that the rod could pass through it and through the hollow neck. By enlarging this opening along the sagittal suture, flexion of the head on the rod was permitted. Shorter transverse openings in the top of the rubber head allowed some lateral flexion on the rod. A knuckle joint in the neck aided these movements, especially flexion and extension. It was only after these changes had been made in the rubber head that the pelvic curve could be determined. The chain connecting the head to the pelvis was discarded. The rubber shoulders were removed because they were in the way, inasmuch as this head does not really flex on the shoulders at the neck, as is the case in the living fetus. For when the attempt is made to flex the head the rubber shoulders are projected posteriorly because the neck does not bend easily. As the head passes down this curved rod, one can demonstrate its positions and course in normal and abnormal vertex labors and in breech deliveries. Attempts to practice forceps deliveries with this modified rubber head on the pelvic curve rod were not wholly satisfactory. In fact, the best head for forceps work proved to be the leather-covered wooden head of the American-made doll. Recently a spring action has been inserted in the neck of this doll so that it is no longer flaccid. Still more recently

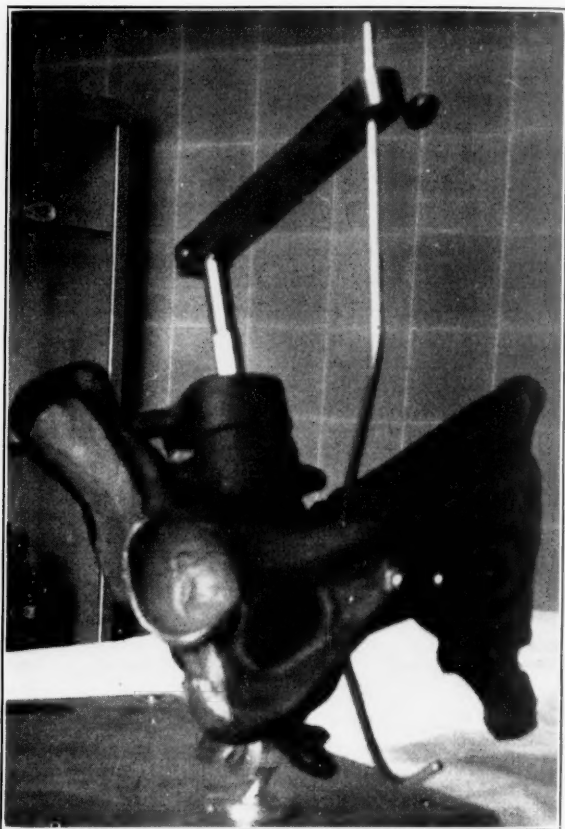


Fig. 1.—Rubber-lined Stander pelvis with bar-holding rod fashioned to pelvic curve.

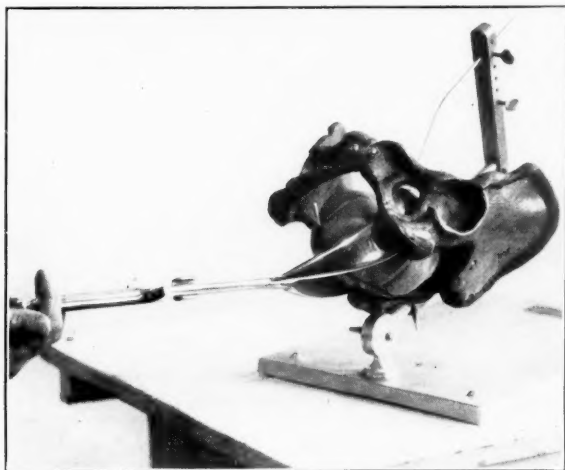


Fig. 2.—Forceps on rubber head in pelvis.

a yielding moldable head with the landmarks preserved has been substituted for the wooden head, to more nearly approximate conditions in the human fetus.

A demonstration possible with this pelvis is the modified Scanzoni maneuver in rotating occipitoposterior positions of the head. Here the forceps blades rotate on their long axis while one observes the sweep taken by the handles. A forceps must be sacrificed for ordinary use by having two bars fastened between the blades in the line of their long axis. Then a straight rod (Fig. 3) is run through holes in the centers of these two bars and the forceps blades are rotated on this rod, while the handles sweep around in an arc which Bill has described and pictured clearly. To make this more realistic the rod is attached to the bar above the pelvic inlet so that the forceps blades rotate on their long axis within the pelvis. This demonstration had been attempted in former years by the use of various instruments with obtuse angles, such as a bandage scissors or a greenstick fracture of an applicator or a match. The shorter part, representing the forceps blades, was made to rotate on its long axis; at the same time the longer end swung round like the handles. The bar above the pelvic inlet may be removed quickly at any time so as to allow of better manipulation with a dead fetus or a doll.

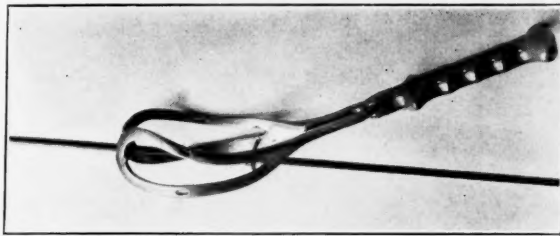


Fig. 3.—Rod through bars in line of long axis of forceps blades.

Since its introduction the Stander obstetric phantom has seemed to be a popular choice. Points in its favor are that it is extremely durable and is not expensive. The modifications of this pelvis here presented make it possible to use with it any forceps without danger of scratching the instrument and allow us to compare different makes of forceps with one another. Other changes permit demonstrations of the modified Scanzoni maneuver and of the descent of the head along the pelvic curve.

Thanks are due to Mr. Joseph P. Faulkner, chief engineer of Mountainside Hospital, to Mr. Wilhelm B. Bronander of the Bronander Engineering and Research Corporation, Arlington, N. J. and to the makers of the pelvis, the Clay-Adams Company, Inc., New York.

21 PLYMOUTH STREET

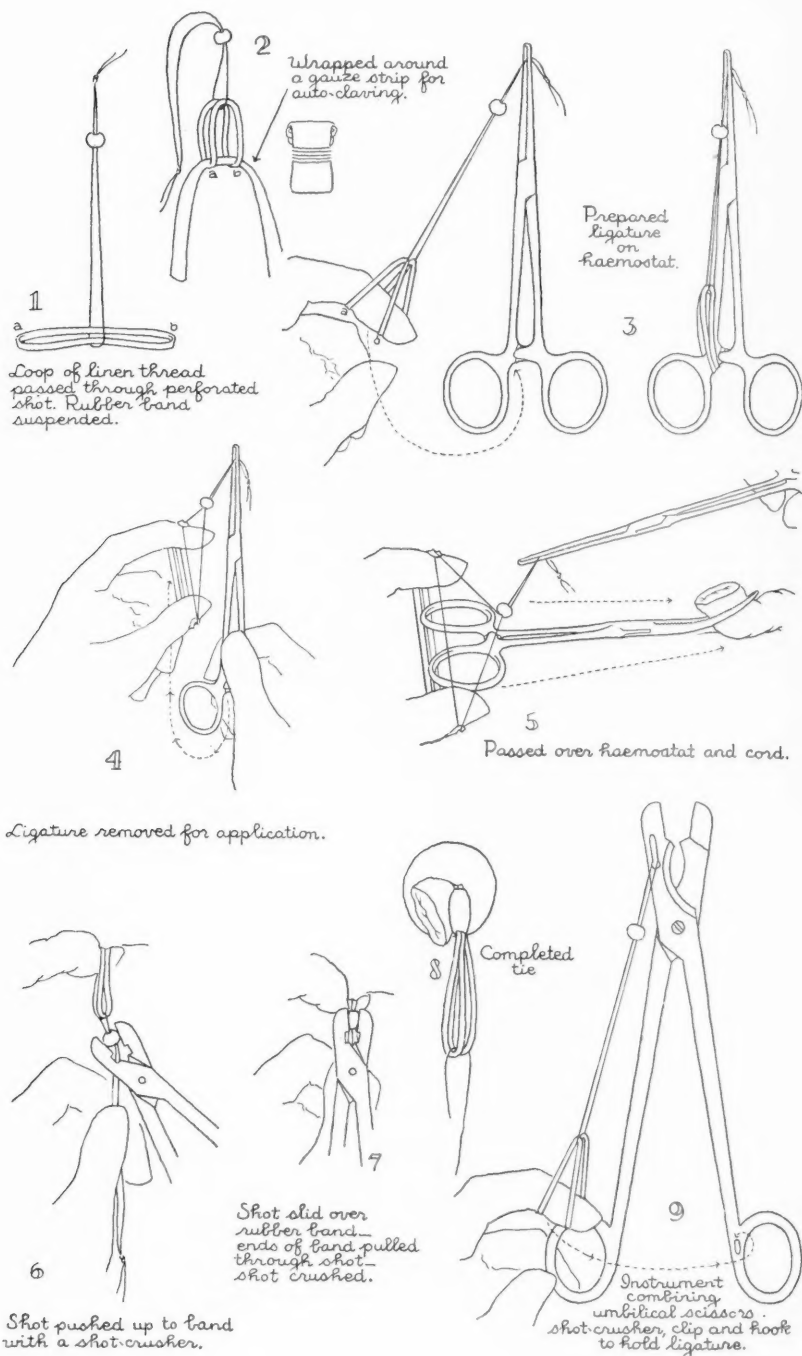
A SIMPLE, SAFE AND ECONOMICAL CORD TIE

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EVERY practicing obstetrician has experienced the need for a comprehensive instrument or appliance to replace ligation of the umbilical cord in the newly born infant, and a careful study of the many varied types already devised revealed none which would adequately satisfy all requirements.

In response to the search for quick simplicity with safety at a minimum expense, a method has been devised by me which has been found to provide all the necessary attributes required of such a tie or clamp. It provides complete asepsis, proper hemostasis with good wound healing, and it permits easy care and dressing. In addition, there is no dangling weight on the cord and it does not cut or tear.



URE

Figs. 1 to 9.

The tie is made of a loop of linen thread, a perforated lead shot and a rubber band, arranged as in Fig. 1. These are wrapped around a piece of gauze for convenience in autoclaving (Fig. 2).

At the time of delivery, the tie is removed from the gauze and arranged as shown in Fig. 3, a hemostat clamping the free end of the thread loop, the rubber band being placed over the handle of the hemostat.

After the umbilical cord is clamped and cut, the rubber band is removed and stretched out with the fingers (Fig. 4). It is passed over the clamped cord and placed as close as possible to the skin (Fig. 5). The shot now is grasped lightly with the shot-crusher and held in a fixed position close to the cord (Fig. 6); and the rubber band is pulled through the perforated shot with a firm and continuous pull on the linen loop (Fig. 7) until the rubber band constricts the cord sufficiently to produce a definite blanching which occurs when enough tension has been applied. The shot is then crushed to hold the rubber tie in place. Thoroughness here is important. The remainder of the cord is cut about one-half inch above the tie (Fig. 8). The ends of the loop may then be cut off or used to hold a cord dressing.

At no time is there any pull on the cord itself. The rubber band does not tear or cut into the umbilical cord and, because it contracts as the cord shrinks, consistent pressure is maintained.

The evolution of this method has prompted the construction of an instrument combining umbilical scissors and shot-crusher with a clip and hook to hold the described ligature (Fig. 9).

In 239 cases* this tie has been used with no adverse results. Separation of the cord occurred naturally on an average of six days after application. This incidence was variable at different institutions where it was applied by internes, nurses, or doctors with differing types of rubber bands and shot. This experience has demonstrated that use of No. 32 rubber band and $7\frac{1}{2}$ mm. lead shot, with 4 mm. perforation, insures the most favorable results. It will readily be appreciated that in this type of tie the quickest separation occurs when the greatest tension is applied.

The cases here cited were observed with parallel application of Zeigler clamps in 77 cases, in which separation occurred on an average of four days; and 50 cases in which umbilicclamps were used, separation occurring on an average of seven days in these cases. Healing is almost identical when this tie or the Zeigler clamp is used, and somewhat more favorable than the umbiliclamp, with which exudate and granulation tissue usually appears.

The newer method here detailed has proved so successful that I believe its trial will convince obstetricians of its economy, efficiency, and complete satisfaction.

*1176 additional patients have been treated successfully without complications since the above report.

Special Article

WILLIAM SHIPPEN, JR.

THE GREAT PIONEER IN AMERICAN OBSTETRICS

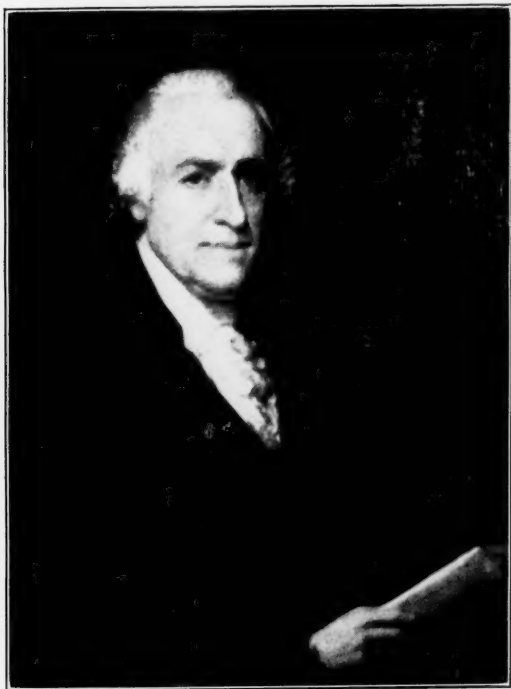
HERBERT THOMS, M.D., NEW HAVEN, CONN.

WILLIAM SHIPPEN, JR., of Philadelphia is the great pioneer in American Obstetrics for he was the first lecturer on that subject in this country and the first to establish a hospital for such instruction. His early course of anatomical lectures, 1762 and 1763, represents in fact the beginnings of medical teaching in America.

Shippen belongs to that comparatively small group of men in medicine who are famous sons of famous fathers. His father of the same name was descended from Edward Shippen, a member of the Society of Friends who emigrated to Boston from Cheshire, England, in 1668. At the request of William Penn this ancestor soon removed to Philadelphia and as first mayor of that city is said to have become distinguished as having three great things: "the biggest house, the biggest person, and the biggest coach." Edward's son Joseph married Abigail Grosse and William Shippen (Sr.) was born to them Oct. 1, 1712. He was wholly educated in his native city and became a leader in medicine in his time. He was the first physician to the Pennsylvania Hospital, a founder of the University of Pennsylvania, and a founder of the College of New Jersey (Princeton University). In 1778 he was elected to the Continental Congress and he was one time vice-president of the American Philosophical Society.

William Shippen, Jr., was one of four sons born to Susannah Harrison and William Shippen, and was born in Philadelphia Oct. 21, 1736. As a boy he attended the Rev. Samuel Finley's academy in Nottingham, Pa. This school was one of the important educational influences in colonial America and its proprietor subsequently became President of the College of New Jersey. Among fellow students of William Shippen at the academy were John Morgan and Benjamin Rush. From Nottingham the young Shippen entered the College of New Jersey, then under the presidency of Aaron Burr, father of the Vice-President of that name. In 1754 he received his bachelor's degree and at commencement was chosen to deliver the valedictory address. The great preacher, George Whitefield, an auditor on that occasion, is said to have been so impressed that he urged the young orator to enter the pulpit. Shippen's mind, however, was set on the profession of his father and he returned to Philadelphia where he studied until 1758 at which time he went abroad to complete his education. According to Watson, quoted by Packard, a letter written by his father at this time to an English correspondent reads, "My son has had his education in the best college in this part of the country, and has been studying physie with me, besides which he has had the opportunity of seeing the practice of every gentleman of note in

our city. But for want of that variety of operations and those frequent dissections which are common in older countries, I must send him to Europe. His scheme is to gain all the knowledge he can in anatomy, physie, and surgery." The young student's "scheme" could hardly have failed in the environment in which he found himself shortly after arriving in England. His first residence in London was in the family of John Hunter who at that time was assisting his brother William in the latter's anatomical theater. By means of this association he became friendly with William Hewson and Sir John Pringle, and also at this time came under the notice of Dr. John Fothergill. Fothergill, born of a Quaker family and a leading London physician, had a great interest in the Pennsylvania Colony and in the newly established Pennsylvania



William Shippen, Jr. (From a portrait in the College of Physicians, Philadelphia.)

Hospital. He was also greatly interested in the young man who was planning to carry the latest teachings of the old world to the new. At the expense of 200 guineas Fothergill employed the artist Rensdyek to execute drawings of anatomical structures. The dissection for this purpose is said to have been made by an anatomist named Jenty and John Hunter is reported to have had a hand in the enterprise. These pastel drawings, eighteen in number, and three plaster of Paris castings of the abdomen of a pregnant woman were presented to the Pennsylvania Hospital and today are among the choice possessions of that institution.

William Shippen had a particular interest in midwifery and attended for a time lectures given by Colin Mackenzie, a one-time pupil of Smellie. Shippen received his medical degree from Edinburgh, the title of his thesis being "De Placentae cum Utero Nexu." While in the northern

capital his opportunities were enriched under the instruction of Munro Primus and Cullen. From the foregoing and what I shall mention in following it seems probable that no young man of colonial America who went abroad to study medicine ever had a richer experience or came into finer contact with the great masters of that day. William Shippen was apparently one of those fortunates who are "born aright in time and place."

After finishing his studies at Edinburgh his desire was to continue studying in France. That country was then at war and this trip was made possible only after his friend Sir John Pringle had secured for him a position as travelling physician to a lady journeying to southern France for her health. He resided for a short time in France and while there apparently met among other notables that genius of literary obstetrics, Laurence Sterne, for in a letter written to David Garriek from Paris in March, 1762, Sterne writes, "This will be put into your hands by Dr. Shippen who has been here some time with Miss Poyntz and is this moment setting off for your metropolis."

While in London Shippen had become engaged to Alice Lee, daughter of the Honorable Col. Thomas Lee, acting governor of the Colony of Virginia. She was the sister of Richard Henry Lee and Francis Lightfoot Lee, both of whom were "Signers." Following the death of her parents she had gone to live with her uncle, Philip Ludwell III, in London. Among the circle of friends whom William Shippen found in this household may be mentioned, Fanny Burney, Dr. Samuel Johnson, Boswell, John Paradise, and his own benefactor John Hunter. His marriage took place April 3, 1762, at the Church of St. Mary Le Strand, Middlesex. Within a few days the bride and groom sailed for America where a new house was awaiting them, a present from William Shippen, Sr. This house, which is still standing at the corner of Locust and Spruce Streets, was to become an important landmark in the history of our country and expresses, says a writer, "the quiet dignity and well being of the life of the early American aristocracy." The Fothergill drawings came to America soon after Shippen's arrival in May, 1762, and the donor in a letter to James Pemberton mentioning Shippen says, "that he is well qualified—that he will soon be followed by an able assistant, Doctor John Morgan, and, that if countenanced by the legislature they will be very useful, and erect a school of medicine." At the time of Shippen's arrival in Philadelphia in practice there besides his father were the brothers Thomas and Phineas Bond, Thomas Cadwalader, John Redman, and Cadwalader Evans.

Shippen's plans for lecturing were not delayed for in a newspaper letter of Nov. 11, 1762, he stated "that a course of anatomical lectures will be opened this winter in Philadelphia for the advantage of the young gentlemen now engaged in the study of physie in this and the neighboring provinces, whose circumstances and connections will not permit of their going abroad for improvement to the anatomical schools in Europe; and also for the entertainment of any gentlemen who may have the curiosity to understand the anatomy of the human frame. In these lectures the situation, figure, and structure of all the parts of the human body will be demonstrated, their respective uses explained, and as far as a course of anatomy will permit, their diseases, with the indications and methods of cure briefly treated of. All the necessary operations in surgery will be performed, a course in bandaging exhibited, and the whole concluded with the explanation of some of the curious

phenomena that arise from an examination of the gravid uterus, and a few plain general directions in the study and practice of midwifery. The necessity and public utility of such a course in this growing country, and the method to be pursued therein, will be more particularly explained in an introductory lecture, to be delivered on the sixteenth instant, at six o'clock in the evening, at the State House, by William Shippen, M.D."

The first course of lectures was attended by twelve pupils. The opposition of the public to dissection was demonstrated on several occasions by the smashing of windows in the house where they were performed. The young lecturer sought to soothe this antagonism by announcing in the press that the bodies so used were those of criminals who had been legally executed and "now and then one from the Potter's Field."

Three years later, in 1765, William Shippen began the first systematic lectures on obstetrics which were given in this country. These were illustrated by the "anatomical plates and casts of the gravid uterus at the hospital." The *Pennsylvania Gazette* of Jan. 1, 1765, carried the following advertisement: "Dr. Shippen, Jr., having been lately called to the assistance of a number of women in the country in difficult labors, most of which were made so by the unskilful old women about them; the poor women having suffered extremely, and their innocent little ones being entirely destroyed, whose lives might have been easily saved by proper management; and being informed of several desperate cases in the different neighborhoods which had proved fatal to the mothers as well as to their infants, and were attended with the most painful circumstances, too dismal to be related! He thought it his duty immediately to begin his intended courses in Midwifery, and has prepared a proper apparatus for that purpose, in order to instruct those women who have virtue enough to own their ignorance and apply for instruction, as well as those young gentlemen now engaged in the study of that useful and necessary branch of surgery, who are taking pains to qualify themselves in practice in different parts of the country with safety and advantage to their fellow citizens." Some idea of the conditions prevailing in the obstetrics of that day may be gained from a statement by Shryock who observes, "Maternity cases were left, in English speaking lands, almost entirely to midwives. Despite the general coarseness of the age, the attendance of men upon maternity cases was held to be most indelicate. The apparent paradox may possibly be explained in terms of matrimonial jealousy and suspicion. Whatever the explanation, the fact remains. And since midwives lacked any scientific training, obstetrics proceeded on the level of folk practice with consequences which may easily be imagined."

Shippen established what was practically a lying-in hospital in providing "convenient lodgings" for a few poor women, "under the care of a sober, honest matron, well acquainted with lying-in women." He also informs his prospective pupils that he will "be able to present each of you with one natural labor at least, and have provided a machine, by which I can demonstrate all kinds of laborious and preternatural labor, and so give every necessary direction to enable you to manage all cases with the greatest safety to mother and child."

On May 3, 1765, the Trustees of the College of Philadelphia having considered John Morgan's project to establish a medical school gave the plan approval and elected him Professor of the Theory and Practice

of Medicine. This was the beginning of the medical department of the University of Pennsylvania. In September of the same year William Shippen was elected Professor of Anatomy and Surgery. Anatomical lectures were given by him regularly until the fourteenth course which was in the winter of 1775 when the War of the Revolution caused their suspension. Wistar says regarding Shippen's manner of teaching, "He went through the substance of each preceding lecture by interrogation, instead of recapitulation, thus fixing the attention of the students—and his manner was so happy, that this grave process proceeded like a piece of amusement." The public interest in Shippen's lectures and demonstrations is shown by a notation in John Adams' diary which reads, "Dr. Shippen carried us into his chamber where he showed a series of anatomical paintings of exquisite art. Here was a great variety of views of the human body; whole and in part. The Doctor entertained us with a clear, concise, comprehensive lecture upon all parts of the human frame. The entertainment charmed me."

In 1779 the legislature repealed the charter of the College of Philadelphia at the time of the creation of the University of Pennsylvania and Shippen became a professor in the new school. In 1783 the charter of the College being restored, for a time he occupied chairs in both schools, and when a consolidation took place in 1791 under the title of the former institution he occupied the chair of anatomy, surgery and midwifery with Caspar Wistar as adjunct professor.

William Shippen's first military position, according to Packard, was that of medical director of the Flying Camp in the Jerseys and as such was under the authority of John Morgan as director-general. A short time after, when Morgan was dismissed as director-general, Shippen was advanced to director of hospitals on the west side of the Hudson River, those on the east side remaining under the authority of Morgan. Subsequently Shippen with the aid of John Cochran, who had seen service as surgeon's mate in the French and Indian wars, outlined a plan of reorganization which was adopted by Congress early in the spring of 1777. On April 11 of that year according to Brown, quoted by Graves, "To the position of Director General, Dr. Philip Turner of Connecticut was at first nominated and elected, but before adjournment a reconsideration was moved, and it was urged with great propriety that the author of the plan had claims, not only of great distinction in his profession, but of previous service, which were superior to those of others. Accordingly a new election being held, Dr. William Shippen received the unanimous vote of all the thirteen states." It is not within the present scope to tell of Shippen's military career. We can but mention his famous court-martial, instigated largely by Rush and Morgan, which resulted in his acquittal on all counts and following which the commander-in-chief publicly thanked him for his excellent service. To those interested in this dramatic and historic episode reference is directed to Gibson's excellent volume on the medical background of the Revolution. Shippen attributed the animosity of both Rush and Morgan to the belief that he had forced them out of military preferment. It is interesting to note with regard to the former that time probably healed these ugly wounds for in Rush's diary of July 11, 1806, it is recorded, "Shippen died today! I attended him in his last illness." Shippen remained as Director General until January, 1781, at which time he resigned and resumed his teaching and practice. In obstetrics he succeeded in combating the prejudice against men in this branch to such an extent that he secured a large clientele.

In 1798 a great tragedy of his life occurred in the death of his only son. Wistar says this "cut the sinews of his exertions, and left him gradually to wither—the amiable victim of paternal affection." He lectured but occasionally after this and his practice declined. However, toward the latter part of his life his interest in medicine seemed to return, and we find an account of him again giving his introductory lecture in new buildings now to a class of nearly four hundred. In 1808, his debility returned and he removed to Germantown where he passed away the eleventh day of July.

The men with whom we associate the word great are usually those whose contributions are of a twofold nature, namely, the things that they did and the lives that they influenced. William Shippen established the teaching of clinical obstetrics in this country and his influence on hundreds of his pupils extended throughout the then settled America. When we consider the conditions which faced him in the doing of this task, we must believe that, as it was said of William Smellie: "Man midwifery was the idol of his heart." In considering Shippen's early establishment of a teaching hospital it is interesting to note that it was not until after his return from abroad that the first institution especially established for instruction in obstetrics was founded in London (1765).

William Shippen, eminent in the establishment of anatomical teaching and the development of military medicine, remains the Great Pioneer in American Obstetrics.

REFERENCES

- Flexner, J. T.*: Doctors on Horseback, New York, 1937, The Viking Press. *Gibson, J. E.*: Dr. Bodo Otto and the Medical Background of the American Revolution, Springfield, Ill., and Baltimore, 1937. *Goodman, N. G.*: Benjamin Rush, Physician and Citizen, Philadelphia, 1934. *Graves, C. B.*: *Ann. Med. Hist.* 10: 1, 1938. *Kelly, H. A., and Burrage, W. L.*: American Medical Biography, Baltimore, 1925. *Middleton, W. S.*: *Ann. Med. Hist.* 4: 440, 1932. *Packard, F. R.*: *Ann. Med. Hist.* 4: 219, 1932. *Paul, J. R.*: *J. Tech. Methods & Bull. Intern. Assn. Med. Museums* 12: 19, 1929. *Pilcher, J. E.*: *J. Assn. Mil. Surg. U. S., Carlisle, Pa.* 14: 60, 1904. Short account of the late Dr. Shippen of Philadelphia, father of Professor Shippen of the Univ. of Pa., written by one of the granddaughters of the deceased. *Med. Repos., N. Y.* 5: 355, 1802. *Shippen, Nancy*: Nancy Shippen—Her Journal Book Compiled and Edited by Ethel Armes, Philadelphia, 1935. *Shryock, R. H.*: The Development of Modern Medicine, Philadelphia, 1936. *Sterne, Laurence*: Letters of, in "The Works of Laurence Sterne," Philadelphia, 1857. *Thacher, J.*: A military journal during the American Revolutionary war, from 1775 to 1783, Boston, 1827. *Thacher, J.*: American Medical Biography, Boston, 1828. *Toner, J. M.*: The Medical Men of the Revolution, Philadelphia, 1876. *Williams, J. W.*: A Sketch of the History of Obstetrics in the U. S. up to 1860, Baltimore, Md. *Wistar, C.*: *Phila. J. Med. & Phys. Sc.* 5: 173, 1822.

Vaccaro, Hugo, et al.: Clinical and Bacteriological Considerations Upon Ovarian Infections, *Bol. Soc. chilena de obst. y ginec.* 1: 237, 1936.

After exhaustive studies the authors came to the conclusion that the amniotic fluid constitutes a very good medium for the growth of micro-organisms. Because of its encapsulation, 91 per cent of 22 specimens of amniotic fluid were found to be sterile. The *Bacillus perfringens* was discovered in 2 of the 22 patients, although they had intact membranes.

MARIO A. CASTALLO.

Department of Maternal Welfare

CONDUCTED BY FRED L. ADAIR, M.D., CHICAGO, ILL.

BIRTH AND MORTALITY STATISTICS

IN A RECENT review of the birth and mortality statistics for the United States, Tandy¹ has pointed out many interesting facts. Especially significant are the comparisons between the statistics for 1915 and 1936. The birth rate (16.7 per 1000 estimated population) in 1936 was lower than in any other year except 1933 (16.5) and consequently over 1,000,000 fewer infants were born than would have been expected had the 1915 rate (25.1) prevailed. The stillbirth rate in 1936 was 34 per 1000 live births which is slightly lower than the rate (36) for the preceding two years. Figures for 1915 are not available for comparison. The infant mortality rate was 57 per 1000 live births, lower than that for any preceding year except 1935 (56). The rate (100) in 1915 was almost twice as high. Had this rate prevailed in 1936, 92,000 more infants would have died during that year. The provisional rate for 1937 is 54 per 1000 live births and indicates that the final 1937 infant death rate will probably be the lowest on record. The neonatal mortality for 1915 was 44 per 1000 live births, while in 1936 it had decreased to 33. Mortality on the first day of life has not decreased and was 15 in both 1915 and 1936. The maternal mortality rate of 57 per 10,000 live births is the lowest ever recorded in the United States. This was the seventh consecutive year in which the maternal mortality rate decreased slightly. Among the 24 countries for which information is available only four have higher rates than the United States. The European countries with the lowest rates are Norway (28 per 10,000 live births, 1935), Netherlands and Italy (30, 1936 provisional rate), Irish Free State (32 in 1937), Sweden (33 in 1934). The differences in procedures for assigning cause of death are not sufficient to account for the rate in the United States which is high as compared with most foreign countries.

The largest number of births, stillbirths and maternal deaths occurred among mothers 20 to 29 years of age, the next largest was among those 30 to 39 and the smallest number among those 40 years or over. The maternal mortality and stillbirth rates by age of the mother, however, are much higher among extremely young mothers and those 40 years or over. The stillbirth rate (67 per 1000 live births) was highest among mothers under 15 years of age and lowest (30) among those from 20 to 29. The highest maternal mortality rate was for mothers 40 years or over (146 per 10,000 live births) the lowest (38) was for mothers 20 to 24 years of age.

Of the infant deaths in 1936, 53 per cent occurred during the first month of life, 47 per cent from the first to the twelfth. Death in the first month was due mainly to natal and prenatal conditions (81.1 per cent). Premature birth (14.64 per cent) was the most common condition designated as the cause of death, while injury at birth (13.6 per cent), congenital malformations (10.4 per cent), and other causes (10.6 per cent) made up the remainder of the natal and prenatal conditions. Respiratory diseases (5.0 per cent), gastrointestinal (2.4 per cent), other specified causes (5.3 per cent), and unknown or ill-defined causes (6.1 per cent) accounted for the 18.9 per cent of deaths due to other causes than natal or prenatal conditions. Among infants who completed their first month of life but died before reaching one year of age, natal and prenatal conditions were much less important (14 per cent). In 1936 respiratory conditions caused 35 per cent of these deaths, gastrointestinal dis-

¹Tandy, Elizabeth C.: *The Child* 3: 85, 1938.

eases 23 per cent, epidemic and communicable diseases 7 per cent, all other specified causes 16 per cent, and unknown or ill-defined 5 per cent. Maternal deaths were caused by puerperal infection (38 per cent), toxemia (23 per cent), accidents of childbirth (13 per cent), puerperal hemorrhage (11 per cent), nonseptic abortions (6 per cent), and other causes (9 per cent).

The growing interest in the problem of stillbirths, neonatal and maternal deaths is leading to many special studies regarding these conditions. More widespread application of the remedial measures already recognized to be of value is producing some decrease in all of these conditions. However, since several large communities have been able to decrease the incidence of maternal and infant deaths and stillbirths far below that of the country as a whole, it indicates that by putting into practice what is already known about the prevention of such fatalities greater reductions in the total number of deaths can be made. Sixty-one per cent of the maternal deaths were due to puerperal infection or toxemia. By the use of aseptic technique and by proper treatment during pregnancy and delivery most of these deaths could be prevented. It is believed that one-half the maternal deaths, one-half of the infant deaths and two-fifths of the stillbirths are preventable. Giving all mothers the full benefit of our present knowledge would save almost 1,000,000 lives each year.

Simon, C.: Chancres of the Uterine Cervix Accompanied by Palpable Pelvic Adenopathy, Presse méd. 55: 1085, 1938.

Recently, in each of three patients with proved chancre of the cervix, the author palpated a firm, spherical, cherry-sized elusive mass in the lateral pelvic wall, and he interpreted this as representing regional adenopathy of the primary lesion. To detect the gland the slightly flexed examining fingers should be placed deeply in the lateral fornix against the osseous surface of the true pelvis and be drawn forward. By means of ingeniously planned x-ray studies it was ascertained that the gland lay approximately 5 cm. from the ischial spine and 2 cm. from the ileopsoas line in a vertical axis passing through the spine. Cadaver dissection verified the clinical and radiologic finding by revealing the presence of a normal lymph node approximately the size of a grain of corn. This node corresponds to the one that Leveuf and Godart described as the "principal ganglion" of the uterine lymphatics. Usually there is a single node, although occasionally there are two.

A thorough review of the world's literature did not reveal any detailed reference to this finding. Fournier, in a description of regional adenopathy in relation to chancre, simply refers to the existence of a "pelvic node" accompanying chancre of the cervix, but parenthetically qualifies it as "theoretical." He adds that except for an occasional bubo there is in general no inguinal lesion. Jeanselme and Lefevre, in their treatise on syphilis, quote the general consensus of opinion that the adenopathy accompanying chancre of the uterine cervix is pelvic, and consequently impossible to detect.

These enlarged pelvic nodes have never been sought because they were always believed to be clinically inaccessible. Simon observed 21 cases of cervical chancre in the past two years, but the thought of searching for the accompanying lymphatic lesion did not occur to him.

This interesting clinical observation confirms the classical belief of Ricord and Fournier in the constancy of the existence of a satellite bubo.

Such an adenopathy may be considered residual evidence of a pre-existing cervical chancre. Knowledge of the fact that the draining lymphatics of the corpus uteri share the efferent vessels of the cervix suggests the possibility of making a diagnosis of intrauterine chancre in the presence of enlargement of this important lymph node.

ARNOLD GOLDBERGER

Society Transactions

NEW YORK OBSTETRICAL SOCIETY

MEETING OF MAY 10, 1938

The following papers were presented:

Ante-partum Rupture of the Uterine Scar Following Low Flap Cesarean Section. Dr. J. Randolph Gepfert (by invitation). (For original article, see page 466.)

A Fifteen-Year Study of Cesarean Section at the Woman's Hospital of New York. Dr. Ralph L. Barrett. (For original article, see page 434.)

CHICAGO GYNECOLOGICAL SOCIETY

MEETING OF MAY 20, 1938

The following papers and discussions were presented:

The Manchester (Parametrial Fixation) Operation for Cure of Prolapse and Cystocele. Dr. M. L. Leventhal and Dr. L. D. Boshes. (For original article, see page 384.)

Pregnancy With Leucemia. Dr. R. M. Grier and Dr. H. A. Richter (by invitation). (For original article, see page 412.)

Editorials

Narcotic Asphyxia in the Newborn

NINETY-EIGHT per cent of all babies normally born of unnarcotized mothers breathe immediately.¹ Of those born of narcotized mothers, from 30 to 60 per cent, according to the particular narcotics employed, exhibit a more or less prolonged period of apnea. Although the majority are resuscitated, many never breathe;² others succumb within a few days to persisting atelectasis and pneumonia;³ and still others, according to Schreiber,⁴ suffer such degrees and durations of cerebral asphyxia that permanent degenerative changes in the brain and lifelong neurologic defects result.

It is important to distinguish between the asphyxia resulting from narcotics and that induced by the inevitable hazards of birth. One is primarily toxicologic and secondarily anoxic; the other is merely anoxic. To overcome a merely anoxic asphyxia two methods have been employed. The older method applied strong and often harmful sensory stimulation. The baby was dipped in hot and cold water, slapped, kneaded and otherwise "cranked," like a stalled automobile. The other method consists in the inhalation of oxygen and 5 to 7 per cent carbon dioxide.⁵ Higher percentages,⁶ if used at all, should be administered only momentarily and replaced by physiologic percentages as soon as respiration is induced. But when the respiratory center is depressed by narcotics both sensory and inhalational stimulation may be ineffective, and even intratracheal insufflation, a very simple technique once it is learned,⁷ may fail.

Narcotics, all of them, depress the respiratory center of the fetus far more than that of the mother. A dosage that merely quiets her at the time of delivery may render the infant dangerously apneic and lethargic. If any considerable dose of morphine is administered shortly before delivery, an apneic baby is to be expected. The case against the barbiturates, particularly those of prolonged action, is even stronger. The belief that these drugs protect the mother from suffering with less depression of respiration in the child than is the case with morphine is erroneous. The depressant effect of morphine decreases after three or four hours, while that of amytal, for instance, lasts three or four times as long. The depressant effect of morphine can be largely counteracted

¹Irving, F. C., Berman, S., and Nelson, H. B.: *Surg. Gynec. Obst.* 58: 1, 1934.

²Bundeson, H. N., Dahms, O. A., Fishbein, W. L., and Harman, G. E.: *J. A. M. A.* 107: 270, 1936.

³Cruikshank, J. N.: *Child Life Investigations. The Causes of Neonatal Death: Medical Research Council Special Report Series No. 145, H. M. Stationery Office, London.*

⁴Schreiber, F.: *J. A. M. A.* 111: 1263, 1938.

⁵Henderson, Y.: *Adventures in Respiration: Modes of Asphyxiation and Methods of Resuscitation*, Baltimore, 1938, Williams and Wilkins Co.

⁶Eastman, N. J., Dunn, R. B., and Kreiselman, J.: *AM. J. OBST. & GYN.* 36: 571, 1938.

⁷Flagg, P. J.: *Ibid.* 21: 537, 1931.

with carbon dioxide; *that of the barbiturates cannot*: a very important point in relation to resuscitation.⁵

The chief inference to be drawn is that only such narcotics as are of relatively brief action are justifiable in labor, and then only in the early stages. In the later stages anesthetics alone should be used; for anesthetics are drugs of brief action and have relatively slight depressive effects upon respiration. Even with anesthetics precautions must be taken against asphyxia. Particularly in the use of nitrous oxide, the percentage of oxygen with which the gas is mixed should not be allowed to fall below 15 per cent.⁸ Otherwise asphyxial effects, immediate or delayed, effects essentially like those of carbon monoxide asphyxia, may result.⁹

Even with these limitations much may be done to diminish suffering. But the science of pharmacology affords no means of rendering childbirth free from even the slightest discomfort or recollection in the mothers except at the cost of many dead or damaged babies.

Yandell Henderson.

Sulfanilamide in Obstetrics and Gynecology

CHEMOTHERAPY in the treatment of infections has received a tremendous impetus during the past three years. At no time in medical history has such a promising drug as sulfanilamide and its related compounds been placed in the hands of the medical profession for this purpose. Experience, however, has amply demonstrated a wide variety of toxic symptoms that may occur following its use, some of which are no contraindication to the continuance of the therapy while others less often offer a definite indication to stop the administration of the drug. Exhaustive research in bacteriologic, immunologic, chemical, pharmacologic and therapeutic fields is necessary before we understand some of the most fundamental actions of the drug.

Sulfanilamide is absorbed as rapidly or even more rapidly when taken by mouth than when administered subcutaneously and absorption is more rapid when given on an empty stomach. It is rapidly distributed throughout all maternal and fetal tissues including the placenta, liquor amnii, colostrum and milk. The drug is eliminated from the body almost entirely by the kidneys. No definite deleterious effects on the fetus have as yet been described. In general, treatment is more successful if the patient is hospitalized as the drug is tolerated better with the patient confined to bed and dosage can be more accurately controlled. Toxic signs and symptoms are also recognized earlier than in ambulatory patients. It is usually advisable to give sodium bicarbonate by mouth at the same time to prevent the possible development of an acidosis. There is usually no contraindication to other *necessary* medication at the same time, but its therapeutic action should not mask possible toxic symptoms. Because of the rapid absorption and prompt excretion, a

⁵Eastman, N. J.: *Ibid.* 31: 563, 1936.

⁹Courville, C. B.: *Medicine* 15: 129, 1936.

satisfactory blood concentration can only be maintained by fractionating the daily dose and administering the drug every four hours.

Medical history has again repeated itself in that with the discovery of a new therapeutic agent the clinical application has far exceeded the indications of proved value. Our present understanding which may be radically modified in the future suggests the following indications, manner of use and control in our field.

a. In puerperal and postabortal infection accurate bacteriologic examination of the lochia is an essential prerequisite to treatment. This may be done by examining the lochia obtained from within the uterus or if this is impossible a sample may be obtained by a simple vaginal swab. If a hemolytic streptococcus is present in the material examined a diagnosis can usually be made in from twelve to eighteen hours. This is necessary because only from 1 to 2 per cent of patients classified as morbid in a well-conducted obstetric service are found to have a beta hemolytic streptococcus in the lochia while an additional 2 to 3 per cent may harbor an alpha prime strain. Even in institutions where only the more seriously ill patients suffering from puerperal infection are admitted usually not more than one-third are found to have hemolytic streptococcus infections. Experience to date indicates that sulfanilamide is of definite value only in the treatment of puerperal infection due to a hemolytic streptococcus and has but little if any effect on puerperal infections due to the other usual organisms associated with such infections. Adequate dosage (6 to 8 gm. per day) in divided doses *early* in the disease is essential if the infection is serious.

b. Pyelitis before, during, or after labor. Again accurate bacteriologic examination of the urine is necessary prior to treatment. If total fluid intake is restricted to 2,000 c.c. per day, a satisfactory concentration of the drug may usually be attained by the administration of 3 to 5 gm. daily in divided doses. Good results are frequently obtained in infections due to the colon-aerogenes group of organisms so often associated with such infections. *Staphylococcus albus* and *aureus* organisms may also often be quickly eliminated from the urine. Urinary tract infections due to nonhemolytic streptococci and some of the other gram-positive organisms are usually treated more successfully by mandelic acid therapy. Smaller doses than mentioned above may be used successfully to sterilize the urine following the subsidence of the acute infection.

c. Gonorrhea. No chemotherapeutic agent used before the introduction of sulfanilamide has yielded anything like as satisfactory results in the treatment of this infection. Clinical experience to date has indicated certain facts that must be taken into consideration in order to obtain the best results. The treatment should not be started as a rule before the elapse of at least eight to ten days after the initial onset of the disease. A chronic gonorrhea is often more easily cured than the acute disease. Bacteriologic studies by cultural methods offer the only sound method of controlling the treatment and determining when a cure is established. It is quite possible that the discharge may cease and clinical symptoms disappear soon after starting treatment *but the gonococcus may still be present* in the local secretions. Thus, a state of

chronic carrier could in this way be established, which may be a possible, serious menace to society. The drug must be administered in adequate dosage from the start of the therapy and until repeated cultures become negative. There is definite evidence to suggest both from clinical findings and from laboratory data that the gonococcus may gradually be induced to grow in the presence of increasing concentrations of the drug, the phenomenon of becoming "sulfanilamide fast." It is readily understandable how this can take place in the patient if low dosage is employed. The ideal dosage has not as yet been determined; however, present information suggests that the initial daily dose should approximate 5 gm. The drug should be continued possibly with decreased dosage until three negative cultures at two-day intervals have been obtained. Determination of "cure" purely by clinical methods and smear interpretation is of very dubious value. "Permanent cure" criteria must depend largely on repeated negative cultures at monthly intervals following sulfanilamide therapy.

To sum up, it may be claimed that this new drug constitutes a valuable and noteworthy addition to the materia medica, but further research is necessary to determine its action and limitations as well as proper dosage. Certain unfortunate results which have accompanied its employment, largely in unskilled hands, should call for that caution which is so essential for safe and successful results.

—R. G. Douglas.

Announcement

American Association of Obstetricians, Gynecologists and Abdominal Surgeons Annual Foundation Prize

The American Association of Obstetricians, Gynecologists and Abdominal Surgeons announces that the annual Foundation Prize for this year will be \$100.00. Those eligible include only (1) interns, residents, or graduate students in Obstetrics, Gynecology and Abdominal Surgery, and (2) physicians (M.D. degree) who are actually practicing or teaching Obstetrics, Gynecology or Abdominal Surgery.

Competing manuscripts must (1) be presented in *triplicate* under a nom de plume to the Secretary of the Association before June 1, (2) be limited to 5,000 words and such illustrations as are necessary for a clear exposition of the thesis, and (3) be typewritten (double-spaced) on one side of the sheets, with ample margins.

The successful thesis must be presented at the next annual (September) meeting of the Association, without expense to the Association and in conformity with its regulations.

For further details, address Dr. James R. Bloss, Secretary, 418 11th Street, Huntington, W. Va.

Department of Book Reviews

CONDUCTED BY ROBERT T. FRANK, M.D., NEW YORK

Review of New Books

Gynecology and Obstetrics

The tenth volume of *Stoeckel's Handbuch der Gynaekologie*¹ has appeared in three fasciculi of, respectively, 738, 438, and 1008 pages. This tremendous production appears to be from the pen of Stoeckel alone.

The first fasciculus covers the anatomy and function of the urinary tract. He considers ureteral antiperistalsis an artificial product and states that damage to the urethral control of the detrusor and sphincter are always inseparable. The changes occurring during pregnancy, labor and puerperium are taken up. In describing diagnostic methods, very little emphasis is placed on intravenous pyelography. A very full description of congenital anomalies follows. Stoeckel is unconvinced that Hunner's ureteral strictures or elusive ulcers occur, but is willing to search for focal infections. The chapter on cystitis is full, as is the very detailed one dealing with endometriosis of the bladder. Although all the well-known methods of treatment of pyelitis are described, the author does not give any decided personal preference. The rarer conditions of gonorrhea, syphilis and lymphogranuloma of the urethra and bladder conclude this portion.

Fascicle II describes tuberculosis of the genitourinary organs, which is always of the descending type. Ten per cent of all tuberculosis deaths are due to urinary infection. However, in contradistinction to the male, no cross infection from the urinary to the genital tract or vice versa takes place in the female. According to Stoeckel, spontaneous healing of kidney tuberculosis does not occur. Pregnancy is no contraindication to operation for tuberculosis of the urinary tract.

Injuries and fistulas of the urinary tract are next taken up. For incontinence, various sphincter plastics are discussed with particular emphasis on the Stoeckel-Goebell technique. The causation and situation of fistulae, the techniques for their repair including the abdominal route and reconstruction of destroyed urethra are described in great detail.

Fascicle III covers ureter fistula and a very minute discussion of the precautions advocated to avoid ureter injuries during vaginal as well as abdominal operation. In special instances, placing the kidney out of function by means of x-ray has been advocated for the relief of ureteral fistula. The author takes no decided stand as to the advisability of this measure. In transplantation of the ureter, Stoeckel prefers the intraperitoneal route with transplantation into the sigmoid. The discussion likewise covers foreign bodies in the kidney, ureter, and bladder. Other subjects are prolapse of the urethra and bladder, tumors of the genitourinary tract, including those of the ureter and bladder. Radical cystectomy is thoroughly discussed and beautifully illustrated, likewise treatment of malignancy with radium and x-ray. The causes of hematuria as well as tumors of the ureters, pelvis, and kidney, are described; the discussion of kidney tumors is limited to the author's personal experience. The reader being referred to books on urology for more extensive descriptions. A very closely printed condensed bibliography covering 320 pages closes the last fascicle.

¹*Stoeckel's Handbuch der Gynaekologie*. Dritte, voellig neubearbeitete und erweiterte Auflage. Zehnter Band. Gynaekologischer Beitrag zur Urologie von Dr. W. Stoeckel, Universitaet Berlin, vol. I, 738 pages with 432 illustrations; vol. II, 438 pages with 261 illustrations; vol. III, 1,008 pages with 468 illustrations. Verlag von J. F. Bergmann, Muenchen, 1938.

This tenth volume is a tremendous contribution, particularly when considered that it comes from the pen of a single author. There are more than 1100 illustrations of which a large number are in color. Of particular beauty are the colored cystoscopic drawings. It is to be regretted that the author has seen fit to keep himself so sedulously in the background, as with his own huge personal experience, most readers would probably have preferred a more subjective presentation. However, these monographs must be considered an extremely valuable contribution to gynecologic and urologic literature.

—R. T. Frank

The *Essentials of Obstetrical and Gynecological Pathology*² by Marion Douglass and Robert L. Faulkner is a brief monograph in which sufficient text is given to explain the numerous illustrations. Its object is to explain by formal training the pathology of gynecology and obstetrics to the house staff and students. The monograph covers the subjects most adequately in briefest compass. The illustrations are excellent and well selected. This booklet is to be highly recommended for the purpose aimed at.

—R. T. Frank

The third edition of Curtis' *Textbook of Gynecology*³ has appeared. This is the third edition in eight years. In this edition anatomy and physiology have been introduced. Most beautiful and accurate anatomic drawings accompany this portion of the text. The endocrine glands have been taken up in detail as far as these apply to the gynecologic sphere, and although these chapters are purposely short, good judgment has been shown in summarizing the latest knowledge and presenting it in understandable form.

This book is distinguished by its conciseness without sacrifice of completeness and readability. The bibliographic references have been chosen with a great deal of judgment. Curtis' textbook will prove of use not only to the student and practitioner but to the specialist who will find much of interest within its pages.

—R. T. Frank

The Book Review Department of the AMERICAN JOURNAL OF OBSTETRICS & GYNECOLOGY takes pride in promptly reviewing such books as are received. According to a letter received recently with *Gynecological Operations*⁴ by Fox and Ibarra, a copy was sent for review in 1936 but did not reach our office. This will explain the review of a book published two years ago.

This textbook on gynecologic operations is complete, showing various incisions, both abdominal and vaginal. In perineorrhaphy the levators are exposed and sutured by one technique although other techniques such as the Tait flap splitting are likewise described. Vulvectomy, both the simple and the more radical operation, with removal of the inguinal glands en masse, is given. Bladder fistulas, ureteral transplantation, the formation of an artificial vagina by means of Pallazo's technique (utilization of the labia) as well as Baldwin's operation are described.

In supravaginal hysterectomy both what they call the American method, in which the bladder is first liberated before tying the uterine arteries, and the French technique, in which this step is not performed, are described. Varicocele of the broad ligament is depicted. A thorough description of the Wertheim operation for carcinoma, with every step indicated, will be found.

This book has a running text, is extremely detailed, well executed with ample illustrations for every operative step. The format is faultless.

—R. T. Frank

²*Essentials of Obstetrical and Gynecological Pathology*, with Clinical Correlations. By Marion Douglass, M.D., Assistant Professor of Gynecology, Western Reserve University, and Robert L. Faulkner, Senior Clinical Instructor in Gynecology, Western Reserve University. With 148 illustrations, 187 pages. The C. V. Mosby Company, St. Louis, 1938.

³*Textbook of Gynecology*. By Arthur Hale Curtis, M.D., Professor and Chairman of the Department of Obstetrics and Gynecology, Northwestern University Medical School, etc. Third edition, reset; 603 pages with 318 illustrations. W. B. Saunders Company, Philadelphia, 1938.

⁴*Ginecologia Operatoria*. Indicaciones y tecnica. Par Eduardo A. Fox y Jose A. Ibarra. Servicio del Hospital Rivadavia, Buenos Aires. Ancieto Lopez, editor, Buenos Aires, 1936.

DeLee's *Principles and Practice of Obstetrics*⁵ has appeared in its seventh edition, in itself not a surprising fact but actually a most noteworthy achievement. This volume now has reached the respectable age of twenty-five years and during this quarter of a century has consistently remained in the front ranks among all textbooks on obstetrics. Each succeeding edition has not only proved the thorough familiarity of its author with all progress in this special field of medicine but as well has demonstrated how much of this progress is due to DeLee's own investigations and observations.

Addition of new material, elimination of obsolete matter, changes in the illustrations and the rewriting of various chapters necessitated resetting of the entire book in this seventh edition.

—Hugo Ehrenfest

*Diseases of Women*⁶ by Ten Teachers, edited by Clifford White, is a sixth edition. Three new authors have taken the place of others, Messrs. Goodwin, Gilliatt, and Wrigley.

The text is short, simple and very well illustrated. Completely rewritten are the chapters on the physiology and disorders of menstruation. A short chapter on contraception and sterility has been put into this new edition. On the whole the methods advocated are current in this country. In perineorrhaphy, suture of the levator muscles is still advocated although this gives a painful, nonresilient perineum in many instances.

—R. T. Frank

The Health Organization of the League of Nations has gotten out a small handy *Atlas*⁷ illustrating the division of cancer of the uterine cervix into four stages, according to the anatomic clinical extent of the growth. The short introductory texts are in English, French, and German. The charts are simple outlines of the pelvis in its three dimensions and for each stage the various possible sites of carcinoma are plainly indicated in red. This *Atlas* should be of great help in making international statistics classifiable and concordant.

—R. T. Frank

A short monograph on the cycle occurring in the vaginal mucosa of the human being by G. di Paola⁸ is based on biopsies obtained from 71 patients, which include children, mature and pregnant women, and after the climacteric. Vaginal smears were likewise made. The author found no regular cycle. He agrees with Lindeman and Stieve that the differences noted are ascribable to desquamation and repair. In pregnancy the changes are not sufficiently pathognomonic to warrant a diagnosis. In the menopause the regressive changes are progressive. Injection of estrogens produced marked changes in the climacteric vagina. The vaginal threshold to estrogen is much lower than the endometrial threshold.

—R. T. Frank

Casas' short monograph on *Leucoplakia of the Vulva*⁹ is based on twenty cases seen in ten years. The ages of the patients were between forty and sixty-five years. He prefers surgery followed by estrogenic therapy to any other treatment. This is a short, well illustrated and complete monograph containing nothing new.

—R. T. Frank

⁵*The Principles and Practice of Obstetrics*. By Joseph B. DeLee, Professor of Obstetrics and Gynecology, emeritus, University of Chicago, etc. With 1,277 illustrations on 985 figures, 271 of them in color, 1,211 pages. Seventh edition, entirely reset. W. B. Saunders Co., Philadelphia, 1938.

⁶*Diseases of Women*. By Ten Teachers, under the direction of Clifford White. Edited by Sir Comyns Berkeley, Clifford White and Frank Cook. Illustrated, 492 pages. Sixth edition. William Wood & Company, Baltimore, 1938.

⁷*Atlas* (English). Illustrating the division of cancer of the uterine cervix into four stages. (Francis) Sur la division des épithéliomas du col de l'utérus en quatre stades. (Deutsch) Über die Einteilung der Kollum-Karzinome des Uterus in vier Stadien. J. Heyman, M.D. Radiumhemmet, Stockholm. League of National Health Organisation. Inquiry into the Results of Radiotherapy in Cancer of the Uterus. Stockholm, 1938. P. A. Norstedt and Söhner.

⁸*El Cielo de la Mucosa Vaginal en la Mujer*. Par Guillermo di Paola. Illustrated, 76 pages. Editor: El Ateneo, Buenos Aires, 1938.

⁹*Leucoplasia de la Vulva*. Par Pedro Figuerosa Casas, professor adjunto de Clinica Ginecológica de la Facultad de Ciencias Médicas de Rosario, etc. Liberia y editorial Ruiz, Rosario, 1937.

Evolving from a series of staff lectures in his hospital, Dr. Falk publishes his lecture material in *Practical Clinical Gynecology*.¹⁰ This material has previously appeared in serial form in the *American Journal of Surgery*. In successive chapters he defines, discusses, and illustrates the methods of examination and the technique employed in treating pelvic pathology in his service at the Harlem Hospital. Two chapters are devoted to the examination of the patient and operative routine, after which the various major subdivisions of gynecologic diseases are taken up in brief fashion as to pathology, symptomatology, and treatment. Particularly Dr. Falk has defined the indications for operation on his service for these various pathologic conditions. Many of the operative procedures are illustrated. The final chapter describes the technique and methods of the ambulatory or clinic service and discusses minor infections and local procedures.

—Philip F. Williams

Samuel's *Endogen Endocrine Therapy in Gynecology and Etiological Treatment of Carcinoma*¹¹ does not lend itself to serious review.

Quotations from the accompanying announcement to his colleagues will show why I say this. "After my experiments had proved that cancer is caused by the hypophysis I succeeded with the aid of the endocrine electrodiagram in demonstrating that carcinoma is invariably a consequence of primary or secondary thyreotropic hyperpituitarism.

"I came to the conclusion that instead of 15 or more hormones being formed in the hypophysis there are only two: the one which accelerates cell breathing, also known as the thyreotropic hormone, and the one which retards cell breathing, the gonadotropic hormone."

The diagnoses are made by means of a modified spectroscope which shows oxyhemoglobin reduction and meth-hemoglobin. The main basis of his theme is that carcinoma is caused through dysfunction of the hypophysis. He claims to cure even liver metastasis with short wave to the hypophysis. In my opinion this appears to be a worthy successor to Abraham's method.

—R. T. Frank

*Der Zyklus der Frau*¹² by Dr. Jules Samuels, written for lay consumption, offers a new method of determining the time of ovulation, presence of pregnancy, and the problems of menstruation with both normal and abnormal women.

The proposed simple examination by which these conditions may be determined is made possible by the use of a new instrument, the "cycloscope." This consists of a spectroscope and a powerful lamp mounted on a stand with an examining platform upon which the patient's hand is to be placed. This test is made by examining the delicate tissue between the thumb and forefinger with relation to the spectroscopic changes in the oxyhemoglobin content of the blood as it passes this point. The reduction time figured by changes in the spectroscopic analysis of the blood viewed through the instrument is believed to bear a very definite relation to the hormone content of the blood of the woman.

—Philip F. Williams

This monograph, *Grundlagen der gynaekologischen Kurzwellentherapie*¹³ has appeared as a supplemental number to the *Zeitschrift für Geburtshilfe und Gynäkologie*, Vol. 117. Dr. Raab explains the fundamental physical principles of the short wave, its differences from other modes of heat production and the explanation of the biologic effects produced in the body through its use. He discusses the possibility

¹⁰*Practical Clinical Gynecology*. By Henry C. Falk, M.D. Clinical Professor of Gynecology, New York University College of Medicine, etc. Illustrated, 393 pages. American Journal of Surgery, New York, 1938.

¹¹*Endogene Endokrinotherapie in der Gynaekologie*. Actiologie und Behandlung des Karzinoms. Von Dr. Jules Samuels, Chirurg und Frauenarzt in Amsterdam, etc. 182 pages. A. W. Sijthoff's Uitgeversmaatschappij, N. V. Leiden, Holland, 1938.

¹²*Der Zyklus der Frau*. Reform Des Ehelebens. von Dr. Jules Samuels, Chirurg-Frauenarzt, Leiter der Einrichtung für Kurzwellentherapie. Haag—G. Naef, Amsterdam, 1938.

¹³*Grundlagen der gynaekologischen Kurzwellentherapie*. Von Dr. med. Ernst Raab, Berlin. With 29 illustrations, 66 pages. Ferdinand Enke Verlag, Stuttgart, 1938.

of harmful influences and methods of application, calculation and indication of certain dosages and the types and technique of the various methods of application through body plates and other forms of electrodes.

Taking up the treatments of gynecologic disorders he discusses the use of this type of therapy, in inflammatory conditions, and mentions its use not only as a curative method but also as a pre- and postoperative help. The benefit of this therapy in noninflammatory conditions is stated. He feels that in some instances short wave treatment of the pituitary gland can be useful in various types of amenorrhea or irregularities of the menstrual cycle. A very good presentation of this form of treatment in gynecologic disorders.

—Philip F. Williams

Dr. Runge presents a second edition of his monograph on *Hemorrhage and Leucorrhea*.¹⁴ The early appearance of this edition has been considered necessary on account of the rapid developments in endocrinology. These advances have been incorporated in the text of the different chapters where such inclusions were pertinent. Runge not only refers to biologic therapy in the different chapters but adds three sections on follicular hormones, corpus-luteum hormones and the gonadotropic hormones, differentiating their qualities and suggesting caution in their therapeutic uses in the disorders of the menstrual cycle. In his discussion he makes a clear differentiation of substitution therapy and stimulation therapy as well as between the estradiol-benzoate and estrin.

There is an excellent short section on the various types of leucorrhea, functional and infective. Runge favors the Sturmdorf operation for the leucorrhea of chronic cervical origin.

—Philip F. Williams

Da Costa's *Lectures on Clinical Obstetrics*¹⁵ form a large volume of 623 pages. The lectures are very complete, show a due spirit of conservatism, and include the modern additions to obstetrics.

The appearance of the book both as to paper and illustrations would not pass muster in this country. The illustrations, where they show position of fetus, are at least understandable, but when attempts are made to show skin and bone lesions of syphilis, they fail completely.

—R. T. Frank

Maternal Care, Marriage, etc.

This small volume, *Maternal Care, Complications*¹⁶ appears as a supplementary text to the treatises on Maternal Care published by the American Committee on Maternal Welfare. The table of contents lists the Toxemias of Pregnancy, Obstetric Hemorrhage, and Puerperal Infections.

These subjects have been correlated by the entire committee as an editorial board, for the benefit, particularly, of the general practitioner who includes obstetrics in his work. It is believed and hoped that this presentation of such important subjects will be a decided help to those engaged in the practice of obstetrics.

—Philip F. Williams

*Season of Birth*¹⁷ represents the continuation of a study begun several years ago by Dr. Huntington on the effect of the time of birth on mental and physical development. The study described in this book examines millions of births in order

¹⁴*Blutung und Fluor.* Von Professor Dr. Hans Runge, Universitäts-Frauenklinik, Heidelberg. Third improved edition, with 17 illustrations. Theodor Steinkopff, Dresden, 1938.

¹⁵*Líções de Clínica Obstétrica.* Par Clovis Correa da Costa, chefe do Serviço de Ginecologia do Hospital da Fundação Gaffree-Guinle. Livraria Moura, Rio de Janeiro, 1938.

¹⁶*Maternal Care, Complications.* Prepared under editorship of Dr. Fred L. Adair, and approved by the American Committee on Maternal Welfare, Inc. University of Chicago Press, 1938.

¹⁷*Season of Birth.* Its Relation to Human Abilities. By Ellsworth Huntington, Yale University. 473 pages with 104 figures. John Wiley & Sons, Inc. New York, 1938.

to determine the reasons for their seasonal fluctuations and the degree to which births at different seasons vary in quality. Dr. Huntington concludes that man has two different optima of temperature—physical and mental, a relic of the glacial period. The second main result of his study seems to give evidence that man inherits an extremely complex and delicate adjustment to climate and weather. He considers that adjustment hinges on four conditions surrounding conception and birth, the dangers of summer heat to the newborn and the curious relation of low temperature to those of unusual mental ability as well as to the time of their conception.

He attempts to show through statistical tables and deductions therefrom, types of climatic influences, a study not only by geographical variations but by sex ratios, birth incidence, the effect of social custom, marriage habits, agricultural and seasonal migrations. He considers the relation of seasons of births by world trend as well as local and political units in the United States and other countries.

Terminally, he proposes that our new knowledge as to season of birth can be of practical use only if we use it in one of two ways, first: by changing the present seasonal distribution of births, and second: to discover the exact conditions which make certain seasons favorable in certain societies and countries and then to take steps to create those conditions at other seasons of the year. Such a bold eugenic plan will probably not be employed for many generations.

—Philip F. Williams

*Biography of the Unborn*¹⁸ by Margaret Shea Gilbert, an account of the development of the human body, represents, in the opinion of a jury selected by the publishers, "the best book on a scientific subject for general reading."

The book is intended for lay reading and records in simple, concise, understandable style the chronologic changes which take place in the development of the human body before birth, as well as a chapter on the physiology of the exit of the fetus from the mother. A chapter on twinning and one on variations in development are included. The easy style, factually clear text and illustrations should render the book thoroughly suitable for the lay audience for which it is intended.

—Philip F. Williams

In this somewhat unusual volume, *The Man Takes a Wife*,¹⁹ Dr. Wile presents a study of man's problems in and through marriage from the standpoint of normal relationships of a sexual, social, and domestic character. Much has been written upon the feminine life cycle from both the normal and pathologic viewpoint, but here for the first time the practical phases of male life are discussed in the hope that men may be enabled to understand themselves better and that the book may serve at the same time as a guide to women in the mutual problems of marital relation.

Dr. Wile discusses the changing social order occasioned by the transformations in recent years in society as a whole. He analyzes the mental and biologic impulses which lead to courtship and marriage, and considers the various readjustments which men must make in marriage and parenthood. He suggests ways and means to diminish the rising divorce rate. The problems of reproduction, and the husband's position and attitude toward them, include the consideration of limitation of family and pregnancy. The book continues through father to child relation, and the position of the father of the family circle.

Dr. Wile develops the subject of adolescence in the offspring and its treatment by parents. The trials and problems of middle age and family life and the necessary marital readjustments of the male climacteric offer a sound interpretation of the peak and decline of man's virility.

This clear discussion of the daily realities of a man's life in the family circle should fulfill the hitherto unsupplied discussion of marriage problems from the masculine angle, and can be read with profit by both husband and wife.

—Philip F. Williams

¹⁸*Biography of the Unborn.* By Margaret Shea Gilbert. Illustrated, 132 pages. The Williams and Wilkins Company, Baltimore, 1938.

¹⁹*The Man Takes a Wife.* A Study of Man's Problems in and through Marriage. By Ira S. Wile, M.D. 277 pages. Greenberg Publishers, Inc. New York, 1937.

*Médecine et Mariage*²⁰ is the product of the Lyons group which publishes bulletins dealing with medical, philosophic and biologic subjects. This present volume deals with a medical problem from philosophic and clerical as well as medical aspects.

Celibacy, marriage, the problems which arise from both conditions in both the normal and abnormal individuals are taken up. Throughout there is a plea for a higher motive than merely sex satisfaction or a race urge to populate the state. It is said that contraception has a bad effect on both man and woman. This book appears to have been written mainly with the object of clarifying the doubts of lay believers.

—R. T. Frank

*Men Past Forty*²¹ by Niemoeller (by the way, he is not a physician) is a well-written brochure intended for the educated layman and dealing with the subject of impotence. The tone of this book is high. Most of the information contained appears fully authenticated. The author draws a rather dark picture of the prevalence of impotence in one form or another after the age of forty.

The sole blot on the "scutecheon" is the list of aphrodisiacs supplied towards the end of the book; it is true, with the recommendation that they should not be employed except under the guidance of the physician. This list, which contains not only the names of the products but the firms manufacturing them, on the whole does not meet any of the criteria which a physician would demand before recommending such a volume to his patients.

—R. T. Frank

This little pamphlet, *Technique of Contraception*,²² takes up the technique of various contraceptive measures, including that practice known as the "safe" period method. Matsner concludes that the method of choice at the present time is the combination of a mechanical barrier and a spermicidal agent.

—Philip F. Williams

Privately printed to promote the aims of the Free Speech League, *A Challenge to Sex Censor* by Theodore Schroeder²³ discusses his personal ideas on the definition of obscenity as developed by himself and those, especially of the judiciary, who have differed in their interpretation and definition from him. The author states that "if lawyers or judges had combined healthy-mindedness, with some psychological intelligence, they would long ago have discovered that they were no longer able to consider the issue of obscenity, as one of art, morals or religion." Whether or not obscenity may be regarded as subjective or entirely objective will likely long remain a moot point. Probably the conflict between Puritanism and broad-mindedness will continue for some time.

Those who are interested in breaking down some remaining barriers may find, to them, plausible arguments in this confused Freudian presentation.

—Philip F. Williams

Endocrine Glands: Vitamins

*The Pituitary Gland*²⁴ is a symposium covering an investigation of the most recent advances. It was presented before the Association for Research in Mental and Nervous Diseases at their 1936 meeting. A large number of well-known investigators and clinicians took part in this symposium. The entire volume covers 764 pages.

²⁰*Médecine et Mariage*. Par R. Biot, H. Bon, F. Dumarest, J. Gate, J. Gaucherand, E. Lancrenon, M. Péhu, W. Riese, G. Thibon, H. Vignes. Groupe Lyonnais D'études Médicales Philosophiques et Biologiques. 254 pages. Librairie Lavandier, Lyon, France.

²¹*Men Past Forty*. By A. F. Niemoeller, A.B., M.A., B.S. Illustrated, 154 pages. Harvest House, New York, 1938.

²²*The Technique of Contraception*. An Outline. By Eric M. Matsner, M.D. Foreword by Frederick C. Holden, M.D. Fourth edition, illustrated, 50 pages. The Williams & Wilkins Company, Baltimore, 1938.

²³*A Challenge to Sex Censors*. By Theodore Schroeder. Privately printed. New York City, 1938.

²⁴*The Pituitary Gland*. An Investigation of the Most Recent Advances. Proceedings of the Association for Research in Mental and Nervous Diseases, December 28 and 29, 1936. Williams and Wilkins Company, Baltimore, 1938.

Like all such joint presentations, it varies greatly in the value of the different contributions. Section I, which deals with the anatomy of the pituitary, is particularly valuable and has engaged the attention of Tilney, Wislocki, A. Severinghaus, and Rioch. This covers both the gross and microscopic anatomy as well as the blood supply of the organ.

Section II deals with the physiology and is more than double the size of the previous section. We will mention only a few contributors: Evans, Hisaw and Fevold, Collip, Engle, Philip Smith, Fluhmann, and Riddle. From this it will become apparent that every phase of physiology has been dealt with.

Section III covers general considerations mainly from the point of view of the clinician. This is, as can be foreseen, the most uneven of the sections. The study of the glands of internal secretion is still in such a fluid state that almost any hypothesis may be discussed and theories changed from day to day.

This contribution, as a whole, is of importance in regard to some of its contents as a source book, in others merely as a temporary point of view. It is well worth studying.

—R. T. Frank

Oppenauer and Dessau²⁵ from Laqueur's Pharmacological Laboratory have sent a reprint which is part of the *Tabulae Biologicae*, Volume 15. These very valuable and easily referred to tables cover the sources, methods of identification and constitution of the sex hormones, including the international units, tests and all derivatives so far obtained. Included are the male, the female and the corpus luteum hormones. The tables give references by number to the appended literature.

Dessau takes up the biologic action of these hormones as seen in plants, cold- and warm-blooded animals. The effect on the metabolism, circulation, sex, primary and secondary sex organs as well as on the other glands of internal secretion are given, also those noted in pregnancy. This is a valuable contribution particularly for those interested in looking up the literature.

—R. T. Frank

Miss Jennie Gregory has written a book on the *A B C of the Vitamins*²⁶ which corresponds in its method of presentation to the *A B C of the Endocrines*.

While this is a clear and excellent presentation, it has not lent itself as dramatically to the pictorial form as the previous book. Vitamin A, the epithelial protective agent; B₁ and B₂ for beriberi and pellagra; the antiscorbutic factor C; the calcifying vitamin D; the sex vitamin E, are depicted in numerous charts. A chapter on experimental methods and the general relationship of vitamins and nutrition conclude this very interesting, useful little monograph.

—R. T. Frank

*Die Vitamine in der Chirurgie*²⁷ is one of the short monographs published in *Vorträge aus der Praktischen Chirurgie*. It contains a clear and understandable summary of what we know about vitamins A, C, D, and B₁. Emphasis is placed upon the closer relationship between hormones, vitamins, and ferments. A lack of vitamin may be due not to deficiency of nutritive intake, but to excess requirements under particular conditions, excess excretion or excess utilization. It is known that there is an increased loss of vitamin C, ascorbic acid, following anesthesia; hypovitaminoses occur from inflammation and in cancer patients. According to the author, vitamin A protects the liver against hyperthyroid action and makes the use of codeine preoperatively unnecessary.

—R. T. Frank

²⁵**Sexual Hormone.** By R. Oppenauer and F. Dessau. 121 pages. Uitgeverij Dr. W. Junk, Den Haag, 1938.

²⁶**A B C of the Vitamins.** A Survey in Charts. By Jennie Gregory, M.S. Foreword by Walter H. Eddy, professor of physiologic chemistry, Teachers College, Columbia University. Williams & Wilkins Company, Baltimore, 1938.

²⁷**Die Vitamine in der Chirurgie.** Von Professor Dr. Erich Schneider, Chirurgische Univ. Klinik, Freiburg i.B. Verlag von Ferdinand Enke, Stuttgart, 1938.

*The Vitamins and Their Clinical Applications*²⁸ by Stepp, Kuehnau, and Schroeder has been translated by Dr. Herman A. H. Bouman. It is published by the Vitamin Products Company. The German publication appeared in 1936.

The contents of this book as far as it covers the knowledge acquired on the vitamins, particularly the chemistry and physiology, is of general interest. The translation in places is cumbersome. Much of general interest is found in these pages and considerable applies particularly to obstetrics and gynecology.

—R. T. Frank

Surgery

*The Therapeutic Problem in Bowel Obstructions*²⁹ is an elaboration of the essay which received the Gross Prize award of the Philadelphia Academy of Surgery. It is a most important contribution to the subject because it gives not only a full survey of the experiments on animals, dealing with the subject of intestinal obstruction, but likewise a detailed account of the clinical features and methods of therapy to be used on patients.

One of the greatest advances has been the prolonged conservative decompression in the treatment of bowel obstruction by means of the modified Levin duodenal tube with continuous suction. This method of treatment is now so standard that its value requires no discussion. Every surgeon will benefit by reading this monograph and every physician will find it worth while to study it. The book is fully illustrated by numerous line drawings and innumerable well-reproduced x-ray plates.

—R. T. Frank

*Spinal Anesthesia*³⁰ by Maxson is a textbook covering the entire subject in great detail. There is a foreword by W. Wayne Babcock who has been one of the main sponsors of spinal anesthesia in this country and whose experience now reaches some forty thousand cases. Maxson gives the historical basis of spinal anesthesia which was introduced by August Bier. He likewise speaks of the trip made to the United States by Jonnesco in 1910 which many of the surgeons still remember.

The entire subject is covered, if anything, in too great detail. The chemistry of the drugs which have been and are employed, is entered into. The innumerable variations in technique are fully described, including a discussion of hypo- and hyperbaric solutions in which the gravitational effects are most marked. The anatomy, indications, dangers, recovery of broken needles and such diverse topics are included.

The author personally uses gravity control, premedication including barbiturate, morphine and atropine. He uses ephedrine prophylactically and novocaine crystals without barbotage.

His point of view is extremely conservative, particularly in selection of cases and makes no exaggerated claims for this method of anesthesia. The book is excellent for reference and for study both for those desiring to learn the technique as well as those who are practicing it.

—R. T. Frank

Friedländer in his *Therapy of Thrombosis*³¹ based his study largely on the compression bandage treatment first proposed by Heinrich Fischer. This short monograph details the author's experience on 2,500 patients, mainly those of the Wiener

²⁸*The Vitamins and Their Clinical Applications*. A Brief Manual. By Professor Dr. W. Stepp, Director of I. med. Klinik, University of Munich, Dozent Dr. Kuehnau, in Wiesbaden, and Dr. H. Schroeder, Associate, I. med. Klinik, Munich. Translated by Dr. Herman A. H. Bouman, Minneapolis, Minn. The Vitamin Products Company, Milwaukee, Wis., 1938.

²⁹*The Therapeutic Problem in Bowel Obstructions*. By Owen H. Wangenstein, M.D., Ph.D., Professor of Surgery, University of Minnesota, etc. 90 illustrations, 360 pages. Charles C. Thomas, Springfield, Ill., 1937.

³⁰*Spinal Anesthesia*. By Louis H. Maxson, A.B., M.D. Practicing Specialist in Anesthetics; Former Chief Anesthetist, Harborview (King County) Hospital, Seattle, Washington. Foreword by W. Wayne Babcock, M.D., LL.D., F.A.C.S. Professor of Surgery, Temple University School of Medicine. With 69 illustrations, 409 pages. J. B. Lippincott Co., Philadelphia, 1938.

³¹*Die Therapie der Thrombose*. Von Dr. Ernst Friedländer mit 27 Abbildungen im Text. Franz Deuticke, Leipzig und Wien, 1938.

Krankenkasse. He claims to have reduced the average morbidity in individual cases from seventy-five days to six days, without a single embolic death. These patients apparently were mainly cases of phlebitis from varicose veins.

In bed patients the posture should favor unhindered venous circulation. The femur should be at an angle of 45 degrees to the hip, the leg being horizontal. A compression bandage is put from the toes upward and then he starts movements against resistance, performed by the patient himself. Outward rotation of the femur, however, is strictly contraindicated. The patients are gotten out of bed very early. The latest was twenty days postoperative. There were no deaths. The average duration of illness was one week. These results are almost incredibly good and well worth careful study.

—R. T. Frank

Volume IV, Part 3, of Peterson's *The Patient and the Weather*³² deals with organic disease, especially surgical problems. "Superficially it links the patient who may be suffering from an acute abdominal condition to the meteorological environment."

The effect of weather on mass metabolic trends, susceptibility to infection (colds, sore throats), gastric ulcer, are only a few of the subjects treasured upon. Postoperative complications, eclampsia, and even ectopic pregnancy are said to be influenced by the meteorologic environment. A mass of statistics, charts and case histories form the text.

—R. T. Frank

In this monograph, *Innere Medizin in der Chirurgie*³³ v. Kress and Kittler discuss the relationship of the important systemic diseases which may be complicated by surgical lesions necessitating operation. They discuss also the complications which may arise in various systems following operation. The first chapter details the preparation for operation of the patient with cardiovascular diseases of various forms, emergencies which may arise during operation and the treatment of the changes in the circulatory apparatus, which may occur postoperatively. There is an excellent chapter on surgery in diabetes, which makes particular reference to preoperative standardization and insulin dosage and postoperative acidosis. In the discussion of surgery on the icteric patient the authors lay stress on the preoperative preparation with vitamins A and C. The respiratory system is considered not only from its intrinsic pathologic physiology complicated by surgery but in addition the authors discuss the different types of postoperative complications, particularly the therapy of postoperative pneumonia and postoperative pulmonary collapse. The final chapter discusses the physiology, pathology, and pre- and postoperative treatment of surgical lesions which are complicated, as in either brain tumor or other nerve lesions, by loss of sleep and the effect of narcosis in the preoperative handling of such conditions.

—Philip F. Williams

Miscellaneous

Dr. Donald Mainland of Dalhousie University, Halifax, has written a book which should be valuable to all medical men who write papers based on statistical or other data, as well as to laboratory experimentalists who are not fully familiar with the present statistical ideas. It is called *The Treatment of Clinical and Laboratory Data*.³⁴

"The primary object of this book has already been stated—to present ideas and some methods that may help the medical or dental clinician who wishes to benefit from his own observation and from a critical reading of statements made by others."

³²*The Patient and the Weather*. By William F. Peterson, M.D. Vol. IV, Part 3. Organic Disease—Surgical Problems. Edwards Brothers, Inc., Ann Arbor, Mich., 1938.

³³*Innere Medizin in der Chirurgie*. Von Dozent Dr. H. Frh. v. Kress, and Dr. W. Kittler, chirurgische Universitäts-Klinik in München, 144 pages. Ferdinand Enke Verlag, Stuttgart, 1938.

³⁴*The Treatment of Clinical and Laboratory Data*. An Introduction to Statistical Ideas and Methods for Medical and Dental Workers. By Donald Mainland, Professor of Anatomy, Dalhousie University, Halifax, Nova Scotia, Canada. With 23 text figures, 340 pages. Oliver and Boyd, Edinburgh, 1938.

The average medical writer does not make adequate allowances for chance in all observations and judgments. The author believes that the statistical technique and methods can be grasped in three or four hours of reading. I must confess that it has taken me much longer to run over this book for the first time but that it well warrants careful and repeated study. The use of statistical methods will prevent many brash and unfounded statements from being accepted. The style is clear and the presentation is such that even those who are not mathematically minded will grasp it if they will study it with care.

—R. T. Frank

*A Textbook of Clinical Pathology*³⁵ edited by Roy R. Kracke has been written by a number of contributors, all of them connected with universities of our South. The work was first undertaken by Dr. Foster M. Johns of Tulane University and was finished at the time of his death in 1936. Since then it has been brought fully up to date. It covers every aspect of clinical pathology. The authors have worked out every detail that the physician requires, beginning with his laboratory equipment, reagents, and methods of technique, including such items as the making and examination of blood smears, venepuncture, blood volume, etc. The diagnostic agglutination tests, clinical chemistry, including liver, urine, and renal function tests are fully described. The examination of sputum, gastric and cerebrospinal fluid, the laboratory tests in syphilis, and, among miscellaneous tests, those for pregnancy, rabies, and allergy are described.

The book is well planned, well edited, well illustrated, and faultlessly gotten out. It should be of real help, particularly for those who only occasionally perform such laboratory tests, although it is full enough to be of real use to the professional laboratory worker.

—R. T. Frank

*A Biological Approach to the Problem of Abnormal Behavior*³⁶ presents an alternative to psychoanalysis. The author feels that neither the failure to satisfy the sex hunger (Freud) nor the failure to satisfy the hunger for approval (Adler) is a fact of sufficient importance to give a basis of a scientific foundation upon which psychopathology can be built. In other words, in contrast to the Freudian, Adlerian, Jungian, or motivistic basis for abnormal behavior, he predicates a strictly mechanistic (physiologic) basis and upon this mechanistic basis he tries to lay the foundation of psychology and psychopathology.

He says "there is no real distinction between our normal mental processes and those which we are accustomed to speak of as abnormal." Normal psychology must be physiologic and abnormal psychology must rest upon normal psychology. During the course of twenty years he has studied particularly fear, pain, anger, pleasure, and laughter. He has assembled many data and accumulated them to build up his theory. To the author's way of thinking, psychoanalysis stands today as the chief obstacle to progress in the study of the abnormal.

Behavior is due to a highly complicated anatomic mechanism (sense organs, nervous systems, muscles, endocrine glands). Defects and limitations of this mechanism of behavior and not unconscious motives and desires produce abnormal thoughts, feelings, and actions. In the present volume of 459 pages he discusses psychophysiology and pathology, leaving what he calls psycho-orthology or the treatment of these diseases, for a subsequent volume. He is willing to concede the physical mechanism and only that. The state of consciousness is an epiphenomenon or bi-product of physiologic reactions that give rise to our actions. He discusses nonadjustment and maladjustment. He claims it is not the details of formulation presented that are important but the principles which have been followed in their construction.

³⁵*Textbook of Clinical Pathology*. Edited by Roy R. Kracke, M.D., Professor of Pathology, Bacteriology and Laboratory Diagnosis, Emory University, etc. With the assistance of twelve outstanding contributors. Illustrated, 567 pages. William Wood and Company Division, Williams and Wilkins Company, Baltimore, 1938.

³⁶*A Biological Approach to the Problem of Abnormal Behavior*. By Milton Harrington, M.D., Psychiatrist, Institution for Male Defective Delinquents, Napanoch, N. Y. 459 pages. Distributed by The Science Press Printing Company, Lancaster, Pa., 1938.

He emphasizes three differences from psychoanalysis. First, the approach. Normal behavior is merely the behavior suited to our needs. Second, the basic concept; every phenomenon results from some action or change acting upon an anatomic structure. Third, evidence, factual or material, which has shaped his theory to fit the facts and not vice versa as he implies is the case in psychoanalysis.

This is a very well-written, carefully thought-out book which without question will arouse interest, discussion and possibly controversy, particularly in neurologic circles. But it is of equal interest to every medical man.

—R. T. Frank

*The Troubled Mind*³⁷ is a study of nervous and mental illnesses which will interest the medical man, the sociologist, and the educated lay reader. It is a mellow and not too technical exposition of the forms which diseases of the mind assume. The text covers fixed idea and reaction, psychoneuroses (manifestations, nature and causes), traumatic hysteria, inhibitions and mental diseases. Innumerable clinical histories illustrate the exposition.

The author warns that the aggressive psychopath who finds his way into public life may lead the way to social unrest, war and revolution. He likewise points out the futility of committing the psychopathic criminal to variable periods of imprisonment according to the gravity of his crime. If the disease cannot be cured he should be committed permanently.

—R. T. Frank

*A History of Women in Medicine*³⁸ is a fascinating discussion of medical women from the earliest times to the beginning of the nineteenth century. The author, Kate Campbell Hurd-Mead, publishes this as the first volume, the second to cover the nineteenth century up to the present time. Although well documented, the book is written in such a fashion that it can be read with equal pleasure by the profession or the laity. It takes up not only medical women, but the customs of the times, male physicians if these were the teachers of the females, lay women who practiced medicine, particularly in the middle ages, and the whole aspects of each century, including not only the customs, living conditions, but the situation of women as a whole. In addition the lives of female practitioners are discussed in detail.

Anyone interested in the history of medicine, in fact in history as a whole, will read this book with a great deal of enjoyment and profit. It is to be hoped that the author will be able to carry out her purpose of publishing a second volume which will bring her up to the present time.

—R. T. Frank

The brilliant career in medical history of Dr. Fielding H. Garrison forms the subject of this biography,³⁹ and the selected letters of his correspondence. Dr. Garrison may be regarded as a pioneer in the development of American Medical History, and he made this subject his life work. While the *Index Medicus*, in recent years known as the *Quarterly Cumulative Index*, is a godsend to the present-day researchers and medical literateurs, there can be no doubt but that Dr. Garrison's labors on these publications will be held in a continuously increasing appreciation by the scholars of coming generations. Chapters on the story of his life depict his work as a biographer and teacher, his intense love of music, his relationship with his fellow-men and his army colleagues. The many selected letters from his correspondence reveal intimately his many interests. The book closes with a bibliography of his writings and the various appendices expressing further his character and activities.

—Philip F. Williams

³⁷*The Troubled Mind. A Study of Nervous and Mental Illnesses.* By C. S. Bluemel, M.A., M.D., F.A.C.P., M.R.C.S. (Eng.). 520 pages. Williams & Wilkin Co., Baltimore, 1938.

³⁸*A History of Women in Medicine. From the Earliest Times to the Beginning of the Nineteenth Century.* By Kate Campbell Hurd-Mead, M.D. Illustrated, 569 pages. The Haddam Press, Haddam, Conn., 1938.

³⁹*Life and Letters of Fielding H. Garrison.* By Solomon R. Kagan, M.D. With an Introduction by Professor James J. Walsh. 287 pages. The Medico-Historical Press, Boston, 1938.

In his *Adventures in Respiration*⁴⁰ Dr. Henderson discusses the modes of asphyxiation and methods of resuscitation. Dr. Henderson pioneered many years ago with Dr. Howard W. Haggard in the treatment of carbon monoxide poisoning by inhalation of carbon dioxide diluted with oxygen. The practical aspect of this method of revival is current in the practice of all obstetricians in the treatment of asphyxiation and narcotized newborn.

For many years Dr. Henderson's theory regarding the relationship of acapnia to postanesthetic and physical depressions was not generally accepted, but today, as he states in his introduction, the acapnia theory has won its way into surgery, as manifested by the carbon dioxide cylinders in every operating room. In this discussion of asphyxia and resuscitation the story is told in simple language as an adventure which Dr. Henderson has experienced. After recounting the theories of the physiology and pathology of carbon dioxide deficiency, acapnia, carbon monoxide asphyxia, and the resuscitation therefrom, a chapter is devoted to the gases of peace and war. Here the horror of one is offset by the spectacular rescues of the resuscitation teams in commercial and civil life.

Of particular interest to the obstetrician should be Chapters 9, 10, and 11, "How Breathing Begins at Birth," "Asphyxia of the Newborn" and "Resuscitation of the Newborn." Dr. Henderson believes that the function of muscle tonus, deficient in the fetus but present at birth in the normal infant is the answer to the question, "Why does the baby begin to breathe at birth?" He states that even days may be required for complete dilatation of the lungs in infants judged to be wholly normal at birth.

He recounts the factors tending toward the production of asphyxia in the newborn and describes four types of asphyxia. He regards the long "narcotized baby" as due to the excessive use of narcotics and hypnotics in present-day American obstetrics. The various measures used in the resuscitation of the newborn are described. The value of oxygen and carbon dioxide and oxygen by the inhalational treatment are stressed, and the objections to the use of these gases are fully answered.

Remaining chapters in the book discuss such other types of asphyxia and alterations in respiration as may be found in postoperative depression, pneumonia, and circulatory failures.

The book, a succinct and easily read résumé of the important researches of Dr. Henderson in this most important subject, merits reading by all whose work comes in contact with the problems of asphyxia and anesthesia.

—Philip F. Williams

This *Textbook of Anatomy and Physiology*⁴¹ may well be considered to have become a standard in nursing education in having reached a tenth edition. Its life span has now attained forty-four years.

In this new edition an effort has been made through the deletion of obsolete material to keep the book of the same general size as heretofore. Recently established work on physiology, vitamins, endocrine secretion, new work on nervous activity and the recent studies of the kidney have been incorporated.

It is stated in the preface of the previous edition that the authors had aimed to include the material outlined in the course in Anatomy and Physiology in the Curriculum published by the National League of Nursing Education. The idea of the comprehensiveness of such a curriculum is afforded through a perusal of the 600 odd pages comprising the subjects of anatomy and physiology discussed.

—Philip F. Williams

⁴⁰*Adventures in Respiration*. Modes of Asphyxiation and Methods of Resuscitation. By Yandell Henderson. Illustrated, 316 pages. Williams and Wilkins Company, Baltimore, 1938.

⁴¹*Textbook of Anatomy and Physiology*. By Diana Clifford Kimber, Carolyn E. Gray, A.M., R.N., and Caroline E. Stackpole, A.M., Associate in Biology, Teachers College, Columbia University. Tenth edition, revised and rewritten. 276 illustrations, 643 pages. The Macmillan Company, New York, 1938.

*Hemorrhoids*⁴² by Marion C. Pruitt is a short monograph on the diagnosis and treatment of this condition. Anatomy and instrumentarium are given in detail. Nupercaine local infiltration anesthesia is preferred. Proper stress is laid upon the importance of accurate diagnosis. The indications for selecting either operation or injection treatment are described. This monograph is short, clear, and well illustrated.

—R. T. Frank

In a review of the preceding twelfth edition of *Osler's Principles and Practice of Medicine*,⁴³ only two years ago, we gave expression to the hope that the untimely demise of its then editor, Thomas McCrea, would not prevent the presentation of an equally excellent edition of this popular textbook in the future. As a pupil of Osler, and colleague and friend of McCrea, the editor of this new thirteenth edition, Henry A. Christian, found a welcome opportunity of continuing the medical tradition of this work. Once again the volume has been partly rearranged and rewritten to include all the recent advance, especially in the field of therapeutics. It has been enlarged by approximately 300 pages.

—Hugo Ehrenfest

This volume comprises a complete consideration of *Clinical Roentgenology of the Digestive Tract*.⁴⁴ Starting with the diseases of the esophagus the succeeding chapters deal respectively with stomach, duodenum, small bowel, colon, etc. The various types of hernia are included, as well as the diseases of the gallbladder and pancreas. Special chapters are devoted to omental, retroperitoneal and mesenteric tumors, peritonitis, pernicious anemia and to the various functional disturbances of the gastrointestinal tract.

The important feature of practically all of the 20 chapters is the x-ray demonstration of the underlying pathology. The roentgen examinations in general follow accepted routine procedures, the results being depicted in excellent cuts and illustrations. The arrangement of references at the end of the chapters is convenient, the index seemingly complete. All through the volume the descriptions of symptoms and findings are concise but clear.

This new contribution to roentgen literature must be welcomed chiefly on account of its completeness and its value for ready reference.

—Paul C. Schnoebelen

The task of keeping *The American Illustrated Medical Dictionary*⁴⁵ abreast with progress must be formidable. The appearance of newly coined terms in modern medical literature progresses with astonishing rapidity, and thus 3,000 new words had to be defined in this edition, requiring 60 additional pages.

The gynecologist will be surprised to learn that in this edition, as far as we know for the first time in any dictionary, a definition of that widely used term "climacterium" appears. A comparison of definitions of other common gynecologic terms in various dictionaries clearly proves the need for more precise gynecologic terminology.

—Hugo Ehrenfest

⁴²**Hemorrhoids.** By Marion C. Pruitt, M.D., Atlanta, Georgia, President, American Proctologic Society, Associate in Surgery, Emory University School of Medicine, etc. With 73 illustrations, including 7 in color, 170 pages. The C. V. Mosby Company, St. Louis, 1938.

⁴³**Osler's Principles and Practice of Medicine.** Designed for the Use of Practitioners and Students of Medicine. Thirteenth edition. Revised by Henry A. Christian, Hersey Professor of the Theory and Practice of Physic, Harvard University; Physician in Chief of Peter Bent Brigham Hospital, Boston. 1,450 pages. D. Appleton-Century Company, New York, 1938.

⁴⁴**Clinical Roentgenology of the Digestive Tract.** By Maurice Feldman, M.D., Assistant Professor of Gastroenterology, University of Maryland, Baltimore, etc. With a Foreword by Julius Friedenwald, A.M., M.D. 358 illustrations and 1,014 pages. William Wood & Co., Baltimore, Md., 1938.

⁴⁵**The American Illustrated Medical Dictionary.** By W. A. Newman Dorland, A.M., M.D., F.A.C.S. Eighteenth edition, revised and enlarged, with 942 illustrations, including 283 portraits, 1667 pages. With the collaboration of E. C. Miller, M.D., Medical College of Virginia. W. B. Saunders Company, Philadelphia, 1938.

Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D.

Selected Abstracts

Menstruation

Lass, Smelser and Kurzrok: *Studies Relating to Time of Human Ovulation*, *Endocrinology* 23: 43, 1938.

Forty-seven women studied through their post-partum period had 194 fairly regular cycles. One hundred and six cycles (55 per cent) were anovulatory or sterile in character, and the bleeding was not true menstruation, since it did not come from a premenstrual endometrium. Eighty-two cycles (45 per cent) were ovulatory in character, hence fertile, and the bleeding represented true menstruation.

J. THORNWELL WITHERSPOON

Hisao, I.: *On the Symptoms of Ovulation*, *Japanese J. Obst. & Gynec.* 21: 22, 1938.

The author interrogating a group of nurses and female medical students at the Osaka Medical College for Women came to the conclusion that women can perceive various symptoms which occur during ovulation. The most frequent among them is leucorrhea, but other symptoms are languor, enlargement of the breasts, distention of the lower abdomen, drowsiness, etc. The symptoms appeared in most cases from the twelfth to the sixteenth days before the next flow. In most instances they persisted for about three days. Only 40 per cent of nurses but 70 per cent of the women doctors and medical students noticed such symptoms of ovulation.

J. P. GREENHILL

Duckles, D., and Elvehjem, C. A.: *Hemoglobin Studies on College Women with Special Reference to the Effect of Menstruation*, *J. Lab. & Clin. Med.* 22: 607, 1937.

It seems to be generally conceded that there are both daily and hourly fluctuations in hemoglobin and that these are more pronounced in women than in men. Whether or not the variation in women can be attributed in part to menstruation, causing an instability of the hematopoietic system and increased physiologic demands for iron, is unknown. In various series reported, some investigators have concluded that increases and decreases in the hemoglobin during the menstrual period were no different from those in the intermenstrual period, while others have reported a blood-destroying activity in women coincident with menstruation.

In the present small series of 7 college women, varying in age from 20 to 27 years, hemoglobin determinations were made daily and in some cases hourly for a period of 52 days covering approximately 2 menstrual cycles for each subject. The authors state that these 7 subjects were all healthy although one was slightly anemic and one was diabetic. All, however, were in a good state of nutrition. The specimens were obtained from the finger tips, the Newcomer method was used and compared with a carefully standardized disc in a colorimeter. The results were as follows: The average hemoglobin for the women in this series is approximately 14 gm. per 100 c.c. of blood and shows daily variations ranging from 13 to 15 gm. Hourly fluctuations in hemoglobin occur which are not consistently

comparable at corresponding hours on different days. The hourly variations are as marked during the intermenstrual period as during the menstrual period. There is usually a diminution in the hemoglobin during menstruation, the amount varying considerably with different individuals. During the postmenstrual phase of the cycle, there tends to be a rise in hemoglobin which continues to increase slightly during the intermenstrual phase.

W. B. SERBIN

Bokelmann, O.: Blood Changes in the Menstrual Cycle, Arch. f. Gynäk. 164: 597, 1937.

There is a definite decrease in both erythrocytes and hemoglobin content during menstruation. During the premenstrual and postmenstrual periods both are increased. The drop during menses is not due to a thinning or dilution of the blood nor to the blood loss. There is also a decrease in thrombocytes during the menstrual phase. The reticulocytes increase during the premenstrual, menstrual, and postmenstrual phases. There is also an increase in bleeding time during the menstrual phase. No definite leucocytic changes could be determined.

RALPH A. REIS

Gebert, Willy: Capillary Function and Menstruation, Klin. Wchnschr. 15: 828, 1936.

Gebert discusses the various circulatory changes which are found as regular accompaniments of the menstrual cycle such as the premenstrual migraine, premenstrual rise in blood pressure and vicarious menstruation, etc. An attempt was made to study the capillary changes during the menstrual cycle, as it seemed these changes might be important in the understanding of premenstrual migraine and the various types of intracranial bleedings which accompany menstruation.

He therefore investigated the changes in the dermographic latent period and found that capillary function is directly influenced by the various changes associated with the menstrual cycle. There is a definite decrease of the dermographic latent period during the immediate premenstrual days which is followed by a marked rise which reaches its peak with the onset of the menstrual flow. Following this peak there is a rapid falling off until the latent period reaches the normal level again. This occurs as the menstrual flow ends. This premenstrual rise must be due to a spastic condition of the capillary bed.

RALPH A. REIS

Mazer, Charles, Israel, Leon, and Kacher, Leon: Pseudomenstruation in the Human Female, Surg. Gynec. Obst. 65: 30, 1937.

Cyclic uterine bleeding, clinically indistinguishable from a normal menstrual flow, but coming from an endometrium totally lacking the usual secretory changes, occurs in 30 per cent of sterile women who present no abnormality.

The condition is rarely encountered in fertile or potentially fertile women.

The condition may be due to failure of ovulation, a developmental or acquired lack of responsiveness of the uterus to a normal ovarian activity or to a quantitative or qualitative disharmony between the two ovarian hormones, estrin and progesterin.

When the diagnosis is based on endometrial findings alone, the term "pseudomenstruation" is preferable to "anovular menstruation" because the presence of the latter cannot be proved without concomitant study of the ovaries.

WM. C. HENSKE

Gillman, Joseph: Experimental Studies on the Menstrual Cycle of the Baboon, South African J. M. Sc. 2: 156, 1937.

Hartman in 1932 reported that repeated laparotomies and manipulation of the ovaries do not apparently interfere with the course of the menstrual cycle in the *Macacus rhesus*.

Gillman showed in 1935 that both transient and prolonged emotional stimuli do affect the menstrual rhythm in the baboon. In this paper he proves that in the baboon laparotomy and simple examination of the ovaries as well affect the menstrual cycle.

The author concludes that in the baboon, when the ovaries are manipulated near the middle of the cycle, the perineal measurements decrease progressively until the fifth or seventh day after the operation and then increase rapidly. The stages of perineal rest and deturgescence are unaffected. No menstrual bleeding supervenes at the end of the initial drop of the perineum. Unilateral ovariectomy in a young baboon, with short and irregular cycles, results in a development of a normal adult type of rhythm at the end of the third cycle following the operation. Hysterectomy does not permanently affect the perineal rhythm.

F. L. ADAIR AND J. A. HAUGEN

Miller, Arthur G.: The Fertile Period in Practice, Surg. Gynec. Obst. 66: 723, 1938.

A five-year clinical study of the fertile and sterile periods of women has been made. This study quite definitely points out the value of accurate menstrual records as an early diagnostic aid of abnormal female sex organ function. It also shows that ovulation has a definite time relationship to the next succeeding menstruation, and indicates that the time between ovulation and the next menstruation is a matter of fourteen days. This interval does not change with change in rhythm.

The regularity, duration, and character of the menstrual periods are the chief signs of normal or abnormal female sex organ function. Barring accident or disease the menstrual cycle of a normal woman varies continually between a certain maximum and minimum number of days.

That there are definite periods of physiologic fertility and sterility in the menstrual cycles of normal women appears to be a definitely established biologic law.

The fundamental scientific basis of the fertile period procedure is sound and reliable. The procedure offers to mankind, when it is supervised by a physician, a simple, dependable, and physiologic method for conception control.

In the author's clinic every menstruating woman is told of the importance of an accurate menstrual record and is given a suitable card on which to record the dates. Every recently confined woman is instructed as to the importance of spacing pregnancies.

WILLIAM C. HENSKE

Mommsen, H., and Sachs, F.: The Dietetic Influence of Fermentation Arresting Substances Produced During Menstruation, München. med. Wehnschr. 84: 208, 1937.

By means of the method described by Mommsen, the woman's blood is examined during two successive menstrual periods for substances which impede fermentation. The following is thereby established: (1) The inhibiting substance in yeast fermentation of dextrose mounts gradually in the premenstrual phase of the cycle, reaches its maximum shortly before bleeding begins, and vanishes rapidly from the blood with occurrence of the flow. (2) The curve representing the inhibiting substances is higher when based on a high animal protein nourishment than on a vegetable diet. This assertion is based upon examinations of women, who during one menstrual period ate an abundance of meat, and during the following period were fed vegetables and fruit. (3) It has been stated that this inhibitory substance, produced during menstruation, is a derivative of cyclopentano-perhydrophenanthrene. The carbon framework of this substance is found in various potent physiologic and pharmacologic bodies (sterine, sex hormones, heart drugs, neutral saponin).

C. E. PROSHEK

Jenkins, Penelope M., Gunn, Donald L., and Gunn, Alistair L.: Menstrual Periodicity: Statistical Observations on a Large Sample of Normal Cases, J. Obst. & Gynaec. Brit. Emp. 44: 839, 1937.

The authors analyze accurate data compiled from questionnaires and record cards from 770 of 852 women who cooperated in the study.

They conclude that the term "regular" has no precise meaning in connection with menstruation. No cases were found which did not vary by at least 2.75 days between the longest and shortest intervals within the year.

The average interval between onsets of menstruation was 29 days; the commonest averages lay between 26 and 29 days; 90 per cent of patients had an average interval between 25 and 36 days inclusive; in 3 per cent it was more than 37 days and in 7 per cent less than 25 days.

A progressive decrease in average interval was noted with increasing age, amounting to about one day for each 5 or 6 years.

No relationship to marriage, occupation, season, or lunar references was noted.

The variability of menstrual intervals is discussed with relation to the Knaus-Ogino safe period method of contraception.

SAMUEL D. SOULE

Wollner, Anthony: The Physiology of the Human Cervical Mucosa, Surg. Gynec. Obst. 64: 758, 1937.

There is a distinct menstrual cycle in the cervical mucosa. This structure being under hormonal influence like the endometrium, the intermenstrual phases must be taken into consideration when the histologic findings in the cervix are interpreted. In the premenstrual phase the histologic picture may simulate an inflammatory reaction, and cyst formations may result from hormone action by producing exfoliation of the epithelial lining.

An investigation of the diagnostic possibilities, suggested by the data presented, is now in progress.

WILLIAM C. HENSKE

Burch, John, McClellan, G. S., Johnson, Claud, and Ellison, Eugene: The Diagnosis and Classification of Menstrual Disorders, J. A. M. A. 108: 96, 1937.

Glandular cystic hyperplasia of the endometrium is the result of prolonged continuous secretion of estrogen; it cannot occur in patients whose ovaries contain active corpora lutea. Such an ovarian state is the result of a partial failure of ovarian function. Partial castration as well as partial hypophysectomy in animals led to cystic glandular hypertrophy of the endometrium.

An attempt was made to correlate (in the human being) symptoms of menstrual disorder with the endometrial picture gained by a series of biopsies, but was unsuccessful. No single endometrial picture is characterized by a specific history.

GROVER LIESE

Thorn, George W., Nelson, Katherine R., and Thorn, Doris W.: A Study of the Mechanism of Edema Associated with Menstruation, Endocrinology 22: 163, 1938.

The injection of crystalline preparations of estrone, progesterone, pregnandiol, and testosterone induced the retention of sodium chloride and water in normal dogs. Balance studies in human subjects demonstrated a retention of sodium chloride and water during the intermenstrual as well as the premenstrual phase of the cycle. The onset of menstruation was associated with an increased renal excretion of sodium chloride and water. Normal subjects, in whom no dietary restrictions were imposed, were observed to gain weight during the intermenstrual as well as during the premenstrual phase of the cycle. An increase in appetite and thirst was a striking symptom noted during the premenstrual period. The increase in the secretion of the sex hormones and the increase in appetite and thirst appear to be contributing factors in body weight gain, which occurs during the menstrual cycle.

J. THORNWELL WITHERSPOON

Bernhart: A Case of Hyperemesis of Menstruation, Zentralbl. f. Gynäk. 61: 196, 1937.

Occasional vomiting during menstruation is not uncommon but uncontrollable vomiting is rare. A case of the latter kind is here reported. A thorough examination was made but no cause for the vomiting could be found. On the assumption that the vomiting was hormonal in origin, and in the knowledge that there is a fall in estrogenic hormone content at the time of the menses, the patient was given 10,000 and 50,000 units of estrogenic hormone. The vomiting ceased but recurred. More injections of estrogenic hormone were given until 100,000 units had been administered. This controlled the vomiting.

J. P. GREENHILL

Merriman, B. M.: Endocrine Treatment of Dysmenorrhoea, Malayan M. J. 12: 56, 1937.

Dysmenorrhea is considered as congestive or spasmodic. In the spasmodic type there are two groups: one associated with disorders of uterine structure, and the other with disorders of uterine function. In the former type there is frequently present a myometrial hypoplasia or a prepubescent uterus. In this condition follicular hormone has proved very beneficial in the hands of the author.

Where the uterus is normal in structure, the pain is regarded as due to an abnormality of function or deficient "polarity." In this type the corpus luteum hormone is recommended, as well as in the congestive type, where the pain is premenstrual and is relieved by the onset of bleeding. Corpus luteum injections of 2 mg. twice weekly over the last fourteen days of the premenstruum are given.

F. L. ADAIR AND S. A. PEARL

Leung, N. M.: Dysmenorrhoea Due to Stricture of Ureter, Chinese M. J. 51: 365, 1937.

The author states that if all gynecologic cases would be studied also from the urologic viewpoint, it would be found that a goodly proportion of menstrual pain has a urologic background. Out of 100 cases of chronic ureteral obstruction in women of menstrual age, it was ascertained that 13 had dysmenorrhea caused entirely by the ureteral obstruction, twelve being cured by its removal; also that in 23 cases the urologic symptoms were aggravated at the time of menstruation. He believed that cases of dysmenorrhea should be scrutinized for hints of ureteral pathology before any radical treatment is instituted.

C. O. MALAND

Ford, Frank R., and Guild, Harriet: Precocious Puberty Following Measles, Encephalomyelitis and Epidemic Encephalitis, with a Discussion of the Relation of Intercranial Tumors, Bull. Johns Hopkins Hosp. 60: 192, 1937.

The authors describe two cases of precocious sexual development in young girls following measles, encephalitis, and another case of premature development of the sex organs and of sexual misbehavior in a boy, following epidemic encephalitis.

A survey of the literature seems to indicate that destructive lesions in the region of the pineal body and in the walls of the third ventricle may result directly or indirectly in the syndrome of macrogenitosomia precox. Cases are cited in which this syndrome was associated not only with tumors arising in the region of the pineal body but with tumors of the hypothalamus. The same syndrome is known to follow inflammatory processes, such as meningitis, meningo-encephalitis, and epidemic encephalitis.

The information available at present indicates that the pineal body plays no significant role in the production of macrogenitosomia precox, for this gland is quite normal in many cases in which this syndrome is fully developed, and destruction of the pineal body may be followed by no apparent change in the genital organs. The authors have failed to find a single instance in which definite macrogenitosomia precox has been associated with a verified pinealoma.

C. O. MALAND

Siegert, F.: The Climacterium and Its Treatment, Med. Klin. 33: 561, 1937.

In most instances the climacterium is a physiologic and not a pathologic state. Hence treatment during this period should consist of relieving symptoms which annoy a woman. To accomplish this, great consideration must be given to the woman's psyche. Ordinarily when a diagnosis of "climacteric difficulties" is made we think of "ovarian insufficiency—substitution therapy with ovarian hormones." However, this thought process is correct only when there are such disturbances in menstruation as profuse and prolonged bleeding.

It is possible to influence climacteric bleeding, that is, menorrhagia and metrorrhagia, by means of estrogenic hormone. The latter produces proliferation of the endometrium and improves the contractility of the uterus which leads to a rapid expulsion of the functionalis and thus a diminution in the duration of bleeding. However, it is much more difficult to influence glandular cystic hyperplasia of the endometrium by means of corpus luteum hormone. Hence, from the point of view of differential diagnosis it is important to perform a curettement to determine the type of endometrium which is present.

The author believes that the oral administration of estrogenic hormone is as effective as the parenteral route. He points out that not only may the menstrual disturbances but also the other symptoms, many of which are due to a hyperfunction of the thyroid, be overcome by hormones. This can be overcome by iodine preparations.

Climacteric elevation of blood pressure is best influenced by sedatives combined with ovarian hormones. The arthritis which occurs during the change of life may also be helped occasionally by ovarian hormones.

J. P. GREENHILL

Item

American Board of Obstetrics and Gynecology

Application for admission to the Group A, May, 1939, Board examinations must be on file in the Secretary's Office not later than March 15, 1939. The general oral, clinical and pathological examinations for all candidates, Part II Examinations (Groups A and B), will be conducted by the entire Board, meeting in St. Louis, Missouri, on May 15 and 16, 1939, immediately prior to the Annual Meeting of the American Medical Association. Notice of time and place of these examinations will be forwarded to all candidates well in advance of the examination dates.

Candidates for re-examination in Part II (Groups A and B), must request such re-examination by writing the Secretary's Office before April 1, 1939. Candidates who are required to take re-examinations must do so before the expiration of three years from the date of their first examination. The annual dinner meeting of the Board, to which all diplomates and candidates are invited, as well as their wives and others interested in the work of the Board, will be held at the Congress Hotel, St. Louis, on Wednesday evening, May 17, following the close of the examinations. Application blanks and booklets of information may be obtained from Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania.